(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: HOMA, Fred, L. [US/US]; 3430 Pine Grove Lane, Kalamazoo, MI 49008 (US). WATHEN, Michael, W. [US/US]; 6474 Pepperidge, Portage, MI 49002 (US). HOPKINS, Todd, A. [US/US]; 744 Sarah Street, Galesburg, MI 49053 (US). THOMSEN, Darrel, R. [US/US]; 6916 Willson Drive, Kalamazoo, MI 49009 (US).

(54) Title: A METHOD FOR TREATING HERPES VIRUSES

(57) Abstract: The present invention relates to a method for selecting an anti-herpes viral compound and a method for selectively inhibiting herpesvrus in a human host in need of such treatment. The present invention relates to a method for selecting an anti-herpes viral compound and a method for selectively inhibiting herpsvrus in a human host in need of such treatment.

A METHOD FOR TREATING HERPES VIRUSES

FIELD OF THE INVENTION

The present invention relates to a method for selecting an anti-herpes viral

5   compound and a method for selectively inhibiting herpes viruses in a human host in need of

such treatment.

BACKGROUND OF THE INVENTION

The herpesviruses comprise a large family of double stranded DNA viruses. Eight

10   of the herpes viruses, herpes simplex virus types 1 and 2 (HSV-1 and HSV-2), varicella

zoster virus (VZV), human cytomegalovirus (HCMV), Epstein-Barr virus (EBV), and

human herpes viruses 6, 7, and 8 (HHV-6, HHV-7, and HHV-8), have been shown to infect

humans. Several of these viruses are important human pathogens.

HSV-1 is estimated to affect 100 million people in the U.S. Primary infection of

15   HSV-1 usually occurs between the ages of one and four. Cold sores, the visible symptom,

typically appear at a later age, with 20-45% of the population over the age of fifteen

affected (Whitley, Clin. Intect. Dis., 26:541-555, 1998).

Genital herpes (HSV-2) is the second most common sexually transmitted disease,

with approximately 22% of the U.S population infected with this virus (Fleming 1997).

20   VZV is the causative agent of chicken pox upon primary infection and can recur in

adults as zoster.

EBV results in approximately two million cases of infectious mononucleosis in the

U.S. each year. It can also cause lymphomas in immunocompromised patients and has been

associated with Burkitt's lymphoma, nasopharyngeal carcinoma, and Hodgkins disease.

25   Infection with HCMV often occurs during childhood and is typically asymptomatic

except in immunocompriomised patients where it causes significant morbidity and

mortality.

HHV-6 is the causitive agent of roseola and may be associated with multiple

sclerosis and chronic fatigue syndrome. HHV-7 disease association is unclear, but it may

30   be involved in some cases of roseola. HHV-8 has been associated with Karposi's sarcoma,

body cavity based lymphomas, and multiple myeloma.

These viruses are capable of residing in a latent state within the host. Reactivation

of latent virus results from response to environmental stimuli (ex. UV exposure, stress,

etc.). Infections or recurrence can be life threatening in immunocompromised patients such as AIDS or transplant patients where HCMV can result in retinitis, pneumonia, and gastrointestinal disease.

The increased immunocompromised population has created an unmet medical need

5   for antivirals against herpesviruses because current therapies do not have a sufficiently broad spectrum against this family of viruses and/or they have limited utility due to toxicity. The present invention provides a method for selectively inhibiting herpesviruses DNA polymerase with compounds that have broad spectrum activity. The method offers a distinct advantage in the treatment of patients in need, particularly immunocompromised

10 patients at risk of infection or reactivation by many members of the herpesvirus family.

SUMMARY OF THE INVENTION

The present invention provides a method of selecting compounds that inhibit herpes viruses comprising:

15 a)   measuring IC_{50} of a compound of interest that inhibits a wild type herpes virus,

b)   measuring IC_{50} of the same compound that inhibits a binding domain mutant herpes virus which is the same strain of the wild type herpes virus,

c)   comparing IC_{50} of step a with IC_{50} of step b; and

d)   selecting the compound of interest wherein the IC_{50} of step b is at least 3 times

20   greater than the IC_{50} of step a.

In above method, the order of step a and step b are interchangeable.

The present invention further provides a method of selecting compounds that inhibit herpes viruses comprising:

a)   measuring IC_{50} of a compound of interest that inhibits a wild type HSV-1,

25 b)   measuring IC_{50} of the same compound that inhibits a binding domain mutant HSV-1 which is the same strain of the wild type herpes virus,

c)   comparing IC_{50} of step a with IC_{50} of step b; and

d)   selecting the compound of interest wherein the IC_{50} of step b is at least 3 times greater than the IC_{50} of step a.

30   In above method, the order of step a and step b are interchangeable.

The present invention further provides a method of selecting compounds that inhibit herpes viruses comprising:

a)   measuring IC_{50} of a compound of interest that inhibits a wild type HSV-2,

b)   measuring IC_{50} of the same compound that inhibits a binding domain mutant HSV-2

which is the same strain of the wild type herpes virus,

c)   comparing IC_{50} of step a with IC_{50} of step b; and

d)   selecting the compound of interest wherein the IC_{50} of step b is at least 3 times

5   greater than the IC_{50} of step a.

In above method, the order of step a and step b are interchangeable.

The present invention further provides a method of selecting compounds that inhibit

herpes viruses comprising:

a)   measuring IC_{50} of a compound of interest that inhibits a wild type HCMV,

10   b)   measuring IC_{50} of the same compound that inhibits a binding domain mutant

HCMV which is the same strain of the wild type herpes virus,

c)   comparing IC_{50} of step a with IC_{50} of step b; and

d)   selecting the compound of interest wherein the IC_{50} of step b is at least 3 times

greater than the IC_{50} of step a.

15   In above method, the order of step a and step b are interchangeable.

The present invention further provides a method for selectively treating diseases

caused by herpes viruses in a human host comprising administering a compound to a human

in need of such treatment wherein said compound inhibits herpes viruses by interaction with

the binding domain in the viral DNA polymerase.

20   The present invention further provides method for selectively inhibiting herpes

viruses in a human host comprising administering a compound to a human in need of such

treatment wherein IC_{50} of the compound that inhibits a binding domain mutant herpes virus

is at lease 3 times greater than IC_{50} of the compound that inhibits a wild type herpes virus

which is the same strain as the mutant herpes virus.

25   The present invention further provides a compound for treating herpesviral

infections in a human host wherein IC_{50} of the compound that inhibits a binding domain

mutant herpes virus is at lease 5 times greater than IC_{50} of the compound that inhibits a wild

type herpes virus which is the same strain as the mutant herpes virus.

The present invention further provides a compound for treating herpesviral

30   infections in a human host wherein said compound inhibits the herpesvirus by interacting

with the binding domain in the viral DNA polymerase.

The present invention further provides a compound for the inhibiting of herpesvirus

DNA polymerases wherein serial passage of a wild type herpes virus in the presence of said

compound results in a change of the wild type HSV-1 polymerase at amino acid 823 from valine to alanine.

The present invention further provides a compound for inhibiting herpesvirus DNA polymerases wherein serial passage of a wild type herpes virus in the presence of said

5   compound results a change of the wild type HCMV polymerase at amino acid 823 from valine to alanine and at amino acid 824 from valine to leucine.

The present invention further provides a mutant herpesvirus DNA molecule having a nucleotide sequence selected from a group consisting of SEQ.ID.NO. 1; SEQ.ID.NO. 3; SEQ.ID.NO. 5; SEQ.ID.NO. 7; SEQ.ID.NO. 9; and SEQ.ID.NO. 11.

10   The present invention further provides a mutant herpesvirus polymerase amino acid molecule having an amino acid sequence selected from a group consisting of SEQ.ID.NO. 2; SEQ.ID.NO. 4; SEQ.ID.NO. 6; SEQ.ID.NO. 8; SEQ.ID.NO. 10 and SEQ.ID.NO. 12.

BRIEF DESCRIPTION OF THE DRAWINGS

15   Figure 1 – examples of 4-oxo-DHQ and 4-oxo-DHTP compounds.

Figure 2 – Herpesvirus' polymerases amino acid conserved region.

Figure 3 – Recovered virus after serial passage of HSV-1 in presence of 20 μM of compound No. 17.

Figure 4 – Comparision of Wild HSV-1 and HSV-2 herpesvirus DNA polymerase

20   amino acid sequences alligned by amino acid homology. (Seq. No: 14-19)

Figure 5 – Mutant Herpes Virus DNA and amino acid sequence list. (Seq. No: 1-12)

Figure 6 – Wild HCMV herpesvirus DNA polymerases amino acid sequence. (Seq. No 13)

DETAILED DESCRIPTION OF THE INVENTION

25   A key enzyme in the replication of all herpesviruses is the virus-coded DNA polymerase. Most of the currently available anti-herpes drugs target the viral DNA polymerase. Drugs such as Foscarnet acts by direct inhibition of the viral polymerase. These drugs are non-nucleoside inhibitors of herpesvirus DNA polymerases. Others such as the

30   nucleoside analogs, Acyclovir, Penciclovir and Ganciclovir must first be phosphorylated to the monophosphate forms by virus encoded kinases and, further phosphorylated to triphosphate by cellular enzymes before they are active inhibitors. The triphosphate forms of these nucleoside analogs inhibit polymerases by competing with the binding of natural

triphosphates and their subsequent insertion into growing DNA strands. These drugs are
known as nucleoside inhibitors of herpesvirus DNA polymerases.

One of the limitations of the currently available drugs is that they are active against
only a few of the eight human herpesviruses. For example, Acyclovir and Penciclovir
5   inhibit HSV and VZV replication but have poor activity against CMV.

In order to identify antiviral compounds that would have the potential to inhibit
replication of most of the human herpesviruses, compounds are *in vitro* screened for
inhibitors of herpesvirus DNA polymerase activity. Because portions of the amino acid
sequence of the polymerases are highly conserved within the herpesvirus family it is
10 possible to discover small molecules that inhibit herpesvirus polymerases but not cellular
DNA polymerases. Using this biochemical approach, several new classes of compounds
such as the 4-hydroxyquinoline derivatives (4-HQ), 4-oxo-dihydroquinoline derivatives (4-
oxo-DHQ) and 4-oxo-dihydrothienopyridine derivatives (4-oxo-DHTP) were discovered as
potent, non-nucleoside herpesvirus DNA polymerase inhibitors. *In vitro* polymerase assays
15 and/or *in vivo* cell culture assays have demonstrated that these compounds inhibit HSV-1,
HSV-2, HCMV, VZV, EBV, and HHV-8 replication.

4-Oxo-DHQ and 4-oxo-DHTP are derivatives of formula I
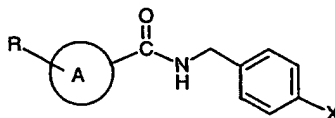
I

20 wherein ring A is a saturated or unsaturated fused double or triple heterocyclic ring having
1, 2, 3 or 4 heteroatoms selected from group consisting of oxygen, sulfur, or nitrogen; and
wherein R and X are the appropriated substitutents, respectively.

Examples of 4-HQ compounds, 4-oxo-DHQ compounds and 4-oxo-DHTP
compounds are illustrated in **Figure 1.**

25 Antiviral activity of these examples are shown in Table 1 below. As shown in Table
1, these compounds inhibit HSV-1 and HSV-2 as well or better than the current
commercially available drug Acyclovir.

Table 1

Antiviral Activity of 4-oxo DHQ/4- xo DTHP Against HSV-1 and HSV-2

Compound IC$_{50}$ (uM)						
virus	1	2	3	4	5	ACV
HSV-1 KOS	2.0	3.8	3.2	3.2	3.3	3.6
HSV-1 F	2.5	2.3	2.2	2.1	2.6	1.3
HSV-1 DJL	2.5	2.6	1.8	2.2	2.7	1.8
HSV-1 Patton	ND	5.3	7.7	4.3	10	9.3
HSV-2 MS	2.0	2.5	2.8	2.5	2.5	10
HSV-2 35D	ND	5.4	5.0	3.2	8.1	6.0
HSV-2 186	2.0	2.3	3.2	2.3	4.2	>10

5   It has also been discovered that point mutations within the HSV-1 polymerase gene

that confer resistance to Acyclovir and other nucleoside analogs do not result in resistance

to the 4-HQ, 4-oxo-DHQs or 4-oxo-DHTPs. Serial passage of wild type HSV-1 in the

presence of 4-oxo-DHQ results in the isolation of mutants that are highly resistant (>20 fold

increase in the IC$_{50}$) to these compounds while retaining sensitivity to nucleoside inhibitors

10   such as Acyclovir.

         In order to determine the mechanism of action of 4-HQ, 4-oxo-DHQ and 4-oxo-

DHTP compounds against herpes viruses, mutants resistant to these compounds are isolated

by serial passage of the virus in the presence of a 4-oxo-DHQ compound. Sequencing

analysis of HSV-1 and HSV-2 strains resistant to the 4-oxo-DHQ identifies that HSV-1

15   (KOS strain) polymerase protein and its homologous HSV-2 have a conserved region (a

binding domain), which is a critical contact point for these compounds. While amino acid

numbering of the DNA polymerase may vary between strains of HSV-1 and HSV-2, this

binding domain encompassing the HSV-1 (KOS) strain amino acid 823 is highly conserved

in herpesviruses and can be identified by alligning the homologous amino acids of this

20   domain as shown in Fig 2.

         In HSV-1 and HSV-2 strains resistant to the 4-oxo-DHQ and similar compounds, a

change of valine to an alanine at the binding domain provides full resistance.

         In the HSV-1 DNA polymerase, resistance is also found when a valine changes to

methionine at amino acid 823 but only when accompanied by a second amino acid change.

25   Isolation of HCMV resistant to 4-oxo-DHQ's is found to be very difficult.

Comparison of the amino acid sequence of the HSV polymerase (Y-G-F-T-G-V-Q-H-G)

and HCMV polymerase (Y-G-F-T-G-V-V-N-G) in the region of amino acid 823

(underlined amino acid) shows that there is a second valine at position 824 in the HCMV

polymerase. In vitro assay using mutant HCMV polymerases demonstrates that full resistance to the 4-oxo-DHQs requires changes at both amino acids 823 (a valine to alanine) and 824 (a valine to leucine). A HCMV polymerase gene containing V823A and V824L mutations is used in marker rescue experiments to generate a viral mutant. This mutant has

5   an IC_{50} approximately 7-fold above that of wild-type HCMV.

The HSV-1, HSV-2 and HCMV mutants are also found to be resistant to other non-nucleoside inhibitors such as the 4-oxo-DHTP and similar compounds. However, when the binding domain mutants (e. g. HSV-1 V823A, HSV-2-MS V826A, HSV-2-186 V828A, and HCMV V823A/V824L mutants) are tested in plaque reduction assays against a series of

10 nucleoside polymerase inhibitors and the non-nucleoside inhibitor such as Foscarnet, replication of the mutants is found to be inhibited by all of the currently marketed anti-herpes polymerase inhibitors tested.

These studies demonstrate that certain non-nucleosides like 4-HQ, 4-oxo-DHQ and 4-oxo-DHTP compounds bind to a different site on the herpes polymerase than the

15 nucleoside inhibitors and Foscarnet. The valine at the binding domain is conserved in the DNA polymerases of six of the eight human herpesviruses and several animal herpesviruses, and appears to play a critical role in the antiviral activity of the 4-HQ, 4-oxo-DHQ and 4-oxo-DHTP compounds. (See **Figure 2**)

Since mutation at the binding domain negates these non-nucleoside inhibitors'

20 activities, compounds could be tested against wild type polymerases and the mutant polymerases to establish the probability of similar binding. We refer to this property of compounds as interaction with the binding domain. Since compounds that interact with the binding domain have exhibited broad-spectrum activity against herpesviruses, this invention provides a method for selecting compounds to treat individuals such as

25 immunocompromised patients who are afflicted with multple herpesvirus infections.

Definitions

The term " wild-type" refers to a gene or gene product which has the characteristics of that gene or gene product when isolated from a naturally occurring source. A wild-type

30 gene is that which is most frequently observed in a population and is thus arbitrarily designated the "normal" or " wild-type" form of the gene.

In contrast, the term "mutant" refers to a gene or gene product which displays modifications in sequence and or functional properties (i.e., altered characteristics) when

compared to the wild-type gene or gene product. It is noted that naturally-occurring mutants can be isolated; these are identified by the fact that they have altered characteristics when compared to the wild-type gene or gene product.

IC$_{50}$ refers to concentration of a drug that inhibits virus growth by 50%.

5   Wild type HSV-1 and HSV-2 strains are listed in **Figure 4**.

Wild type HCMV is listed in SEQ. ID. NO.13.

The term "Iudr" refers to antiviral drug Iododeoxyuridine.

The term "Bvdu" refers to antiviral drug Bromovinyldeoxyuridine.

The term "ACV" refers to antiviral drug Acyclovir.

10   The term "AraC" refers to antiviral drug Arabinosylcytidine.

The term "AraT" refers to antiviral drug Arabinosylthymine.

The term "AraA" refers to antiviral drug Arabinosyladenine.

The term "GCV" refers to antiviral drug Ganciclovir.

The term "CDV" refers to antiviral drug Cidofovir.

15   The term "PFA" refers to antiviral drug Foscarnet.

The term "binding domain" refers to a conserved region in herpesvirus DNA polymerases. The herpesvirus DNA polymerases have seven (7) conserved regions. The binding domain is within the thrid conserved region (see Figure 2). When the binding domain contacts with an inhibitor, at least one amino acid in the binding domain mutates

20   and provides the resistance. In general, the binding domain is at an amino acid sequence position 818-829 of the HSV-1 DNA polymerase or the homologous region in other herpes virus DNA polymerases (see Figure 2).

The term "a binding domain mutant herpes virus" refers to a herpes virus containing a binding domain mutation.

25   More specifically, the binding domain in HSV-1 strains, KOS, F, DJL and Patton are at amino acid sequence position 823. The binding domain in HSV-2 MS-M1 strain is at amino acid sequence position 826. The binding domain in HSV-2 186 strain is at amino acid sequence position 828. The binding domain in HCMV AD 169 strains is at amino acid sequence position 823-824.

30   The term "XxxxY" refers to an amino acid sequence position xxx, a single amino acid X in wild type is changed to an amino acid Y.

For example, the term "V823A" refers to an amino acid sequence position 823, a Valine found in wild type is changed to alanine in mutant strain.

The term "V824L" refers to an amino acid sequence position 824, a Valine found in wild type is changed to Leucine in mutant strain.

The term "V826A" refers to an amino acid sequence position 826, a Valine found in wild type is change to alanine in mutant strain.

5   The term "V828A" refers to an amino acid sequence position 828, a Valine found in wild type is change to alanine in mutant strain.

A table of amino acids and their representative abbreviations, symbols and codons is set forth below in the following Table.

10

Amino acid	Abbrev.	Symbol	Codon(s)					
Alanine	Ala	A	GCA	GCC	GCG	GCU		
Cysteine	Cys	C	UGC	UGU				
Aspartic acid	Asp	D	GAC	GAU				
Glutamic acid	Glu	E	GAA	GAG				
Phenylalanine	Phe	F	UUC	UUU				
Glycine	Gly	G	GGA	GGC	GGG	GGU		
Histidine	His	H	CAC	CAU				
Isoleucine	Ile	I	AUA	AUC	AUU			
Lysine	Lys	K	AAA	AAG				
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG	CUU
Methionine	Met	M	AUG					
Asparagine	Asn	N	AAC	AAU				
Proline	Pro	P	CCA	CCC	CCG	CCU		
Glutamine	Gln	Q	CAA	CAG				
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU
Threonine	Thr	T	ACA	ACC	ACG	ACU		
Valine	Val	V	GUA	GUC	GUG	GUU		
Tryptophan	Trp	W	UGG					
Tyrosine	Tyr	Y	UAC	UAU				

MATERIALS AND METHODS

Cell and Viruses

African green monkey kidney cells (Vero) and human foreskin fibroblast cells

15   (HFF) and herpes viruses can be obtained from the American Type Culture Collection (ATCC). Media is defined as Dulbecco's modified Eagle media (DMEM) containing 10% fetal bovine serum (FBS) and supplemented with antibiotics. Cells are maintained in media at 37°C in a humidified atmosphere of 5% CO^2. HSV-1 strains F, Patton and DJL, HSV-2 strains MS, 35D and 186, and HCMV strain AD169 are used in these studies. Strain DJL is

20   a clinical isolate of HSV-1 isolated in our lab from a primary oral lesion.

Measuring IC$_{50}$ of a Compound of Interest That Inhibits Herpes Viruses

Preparation of Virus Stocks: HSV-1 and HSV-2 stocks are grown in Vero cells. HCMV stocks are grown in HFF cells. Approximately 1 ml of media containing sufficient virus to infect approximately 0.1% to 1% of the cells (multiplicity of infection of 0.001 to

5   0.01 PFU/cell) is added to a T-150 cell culture flask containing a confluent monolayer of cells. The cells are incubated at 37°C for approximately 1 hour. Approximately 50 ml of media is then added to the flask and the cells are incubated at 37°C until viral cytopathic effect (cpe) is apparent in 100% of the cells. The flask is then placed at –80°C for at least 30 min. The flask containing frozen media and cells is placed in a 37°C water bath until the

10   media is thawed. This process disrupts the cells and releases virus into the media. 1 ml aliquots of media containing virus are dispensed into tubes and stored at –80°C. These aliquots of media containing virus are referred to as virus stocks.

Titrating Virus Stocks: Aliquots of virus are thawed at 37°C and serially diluted (10 fold dilutions) in media. 0.1 ml of each dilution of virus is placed in a single well of 24-

15   well cell culture dish containing a confluent monolayer of cells (Vero cells for HSV-1 and HSV-2, HFF cells for HCMV) and incubated at 37°C for 1 h. The virus innoculum is then removed and 1 ml of media containing 0.8% carboxymethylcellulose (CMC) is added to each well of the dish. The dish is incubated at 37°C for approximately 2-3 days (HSV-1 and HSV-2) or 6-9 days (HCMV) to allow sufficient growth of virus to form plaques in the

20   cell monolayer. Plaques can be observed and counted microscopically or by staining the cells with 0.1% crystal violet in 20% ethanol. The virus titer which is expressed as plaque forming units (PFU) per ml is obtained by counting the plaques in a well and correcting for the dilution of the viral innoculum.

Plaque Reduction Assays: Antiviral activity of compounds against herpesviruses such as

25   HSV-1, HSV-2, or HCMV can be measured using plaque reduction assays. 0.1 ml of media containing approximately 50 PFU of virus is added to each well of a 24-well cell culture dish containing a confluent monolayer of cells (Vero cells for HSV-1 and HSV-2, HFF cells for HCMV). Compounds are dissolved in 100% DMSO and diluted in 100% DMSO as 200x stocks of the desired final drug concentration. Typically 5-6 two-fold dilutions are

30   prepared for each compound. Dilutions of compounds are then added to media containing 0.8% CMC resulting in a final 1x drug concentration. After the virus-infected cells have incubated for 1 h at 37°C, the virus innoculum is removed and 1 ml of media containing 0.8% CMC and the various concentrations of compound is added to each well of the dish.

The dish is incubated at 37°C for approximately 2-3 days (HSV-1 and HSV-2) or 6-9 days (HCMV) to allow sufficient growth of virus to form plaques in the cell monolayer. Plaques can be observed and counted microscopically or by staining the cells with 0.1% crystal violet in 20% ethanol. Virus inhibition is determined for each drug concentration by

5   comparing the number of plaques in drug-containing wells to control wells that did not contain drug. Antiviral activity of a compound is expressed as the concentration of compound predicted to reduce the number of plaques in a well by 50% (IC_{50}). The IC_{50} values are calculated by plotting the per cent inhibition vs. concentration of compound using EXCEL software for linear regression.

10

Selection of 4-oxo-DHQ resistant HSV-1 and HSV-2

Vero cells are plated out at a density of 3.5×10^5 cells per well in a six well tissue culture plate. Cells are infected with HSV-1 KOS at a multiplicity of infection (moi) of 0.1 pfu/cell and 1 h post infection the cells are overlayed with 3 ml media containing 20

15   uM of a 4-oxo-DHQ. Cultures are incubated for 20 h at 37°C, freeze/thawed to release cell-associated virus, and 0.1 ml of culture is used to infect a new monolayer of Vero cells (one passage). Serial passage is repeated seven times in the presence of 20 uM drug. Virus isolates are then plaque purified three times prior to preparation of stocks. Virus recovered from each passage in the presence of compound No. 17 is shown in **Figure 3**. 4-oxo-DHQ

20   resistant HSV-1 and HSV-2 may also be selected by the marker transfer method described below using wild-type HSV DNA and the corresponding mutant HSV polymerase gene.

Marker Transfer of a HCMV Mutation

A plasmid containing the wild-type HCMV polymerase gene is modified to contain

25   the V823A or V823A and V824L mutations using a site-directed mutagenesis Kit (Stratagene Corp.) and following the manufactures's protocol. HFF cells are plated into T25 tissue culture flasks to achieve 80% confluency at the time of the transfection. Wild type HCMV AD169 DNA and plasmid DNA containing the mutant HCMV polymerase gene are mixed at a ratio of 1:2 (2ug of viral DNA to 4 ug of plasmid DNA). DNA's are

30   transfected using superfect transfection reagent according to methods recommended by the manufacturer (Quiagen Inc.). Cells are harvested five days posttransfection, freeze-thawed to release virus and half of the sample is used to infect HFF cell monolayers. Cells are overlayed with media containing 20 uM 4-oxo-DHQ compound 2 (see Figure 1). Serial

passage is repeated seven times in the presence of 20 uM compound 2 and virus isolates are then plaque purified three times prior to preparation of viral stock.

Isolation of HSV and HCMV viral DNA

5   HSV DNA is purified from the cytoplasm of infected Vero cells. Vero cells (50 % confluent) are infected at an multiplicity of 0.01 PFU/cell. At 3-5 days postinfection infected cells (100% cpe) are harvested by centrifugation at 1000 rpm in a Beckman GS-6R centrifuge. The pelleted cells are resuspended in TE buffer and placed on ice for 15 minutes. NP-40 is then added to a final concentration of 0.2% and incubated on ice for a

10   further 15 minutes. The cells are centrifuged at 2000 rpm for 10 minutes in a Beckman GS-6R centrifuge. The supernatant is removed and EDTA is added to a final concentration of 20 mM followed by the addition of SDS to a final concentration of 0.3% and proteinase K to a concentration of 50 ug/ml then incubated at 45C for 2 hours. HCMV DNA is isolated by infecting HFF cells (25% confluency) with HCMV at an multiplicity of 0.1 PFU/cell.

15   Cells and media are harvested 5-7 days postinfection (100% cpe) and subjected to low speed centrifugation to remove intact cells and cell debris followed by a high speed spin to pellet virus particles (2500 rpm's in a Beckman SW28 rotor for 1 hour). Following incubation of the HSV and HCMV samples, 1.5 volumes of saturated NaI is added to the digested extract and the refractive index is adjusted to 1.434 –1.435. Ethidium bromide is

20   added to a final concentration of 50 ug/ml. The samples are loaded into a VTI 50centrifuge tube and spun for 24 hours at 45,000 rpm. The DNA band is harvested extracted three times with n-butanol, then dialyzed against TE buffer followed by a dialysis against 95% ethanol and a final dialysis against TE buffer.

25 DNA Sequencing

HSV-1, HSV-2 or HCMV viral DNA's are sequenced directly using an ABI377 fluorescence sequencer (Perkin Elmer Applied Biosystems, Foster City, CA) and the ABI BigDye PRISMTM dRhodamine Terminator Cycle Sequencing Ready Reaction Kit with AmpliTaq FSTM DNA polymerase (PE Applied Biosystems). Each cycle sequencing

30   reaction contained about 1.0 ug of purified viral DNA. Cycle-sequencing is performed using an initial denaturation at 98°C for 1 min, followed by 50 cycles: 98°C for 30 sec, annealing at 50°C for 30 sec, and extension at 60°C for 4 min. Temperature cycles and times are controlled by a Perkin-Elmer 9700 thermocycler. Extension products are

purified using CentriflexTM gel filtration cartridges (Edge BioSystems, Gaithersburg, MD). Each reaction product is loaded by pipette onto the column, which is then centrifuged in a swinging bucket centrifuge (Sorvall model RT6000B table top centrifuge) at 750 x g for 1.5 min at room temperature. Column-purified samples are dried under vacuum for about 40

5   min and then dissolved in 4 ul of a DNA loading solution (83% deionized formamide, 8.3 mM EDTA, and 1.6 mg/ml Blue Dextran). The samples are then heated to 90°C for two min, and held at 4°C until loading. 1.5 ul of each sample is loaded into a single well of the ABI377 sequencer. Sequence chromatogram data files from the ABI377 are analyzed with the computer program Sequencher (Gene Codes, Ann Arbor, MI), for assembly of sequence

10 fragments and correction of ambiguous base calls. Generally sequence reads of 600-700 bp are obtained. Potential sequencing errors are minimized by obtaining sequence information from both DNA strands and by re-sequencing difficult areas using primers at different locations until all sequencing ambiguities are removed.

The entire coding region of the polymerase genes from both the parent strains and

15 the resistant viruses are sequenced. The DNA sequencing is done using viral DNA as the template thus avoiding cloning of the polymerase genes. The amino acid sequence of the DNA polymerases of HSV-1 KOS, F, Patton and DJL and HSV-2 MS and 186 are compared in **Figure 4**. Amino acids that are identical for the six polymerases are shaded in black while regions where amino acid differences are found are shaded in gray. The amino

20 acid sequence of the four HSV-1 polymerases are essentially identical with only a few minor changes noted between the different HSV-1 strains. The majority of amino acid changes are found when the sequences of the HSV-1 and HSV-2 polymerases are compared.

25 **Isolation and Characterization of HSV-1 and HSV-2 Mutants That Are Resistant To the 4-oxo-DHQ's and 4-oxo-DHTP Compounds**

A panel of viruses consisting of four strains of HSV-1 (KOS, F, DJL, Patton) and three strains of HSV-2 (MS, 35D, 186) are tested in a plaque reduction assay against four different 4-oxo-DHQ compounds (# 1, 2, 4, 5 as shown in Figure 1), and one 4-oxo-DHTP

30 compound (# 3 as shown in Figure 1) and against Acyclovir. The six drugs inhibited replication of the seven virus strains with IC_{50} values ranging from 2-10 µM (Table 1). In order to select for 4-oxo-DHQ resistant mutants, HSV-1 strains KOS, F, and DJL along with HSV-2 strains 186 and MS are serially passaged in the presence of 20 uM compound

1. Following the seventh passage, 4-oxo-DHQ resistant virus from each strain are plaque purified three times and high-titer stocks are made. All of the resistant HSV mutants grew to high titers in Vero cells, indicating that the mutations in the resistant isolates did not significantly impair their growth. The mutants selected with 4-oxo-DHQ compound 1 exhibited >10 fold increase in IC_{50} when tested in a plaque reduction assay against 4-oxo-DHQ compound 1 Data are shown in Table 2.

Table 2

4-oxo-DHQ Resistant Virus of HSV-1 and HSV-2

Virus Mutants	Compound 1 IC_{50} (uM)	Amino Acid Change in HSV DNA Polymerase
HSV-1 Kos-M1	>20	- V823A
HSV-1 F-M1	>20	- V823A
HSV-1 DJL-M1	>20	-V823A
HSV-2 MS-M1	>20	- V826A
HSV-2 186-M1	>20	- V828A

*HSV-1 and HSV-2 isolates grown in the presence of 4-oxo-DHQ select for resistant virus.

DNA sequence analysis of the 4-oxo-DHQ resistant mutants (HSV-1 KOS-M1, HSV-1 F-M1, HSV-1 DJL-M1, HSV-2 186-M1, HSV-2 MS-M1) demonstrated that all five mutants contained a single point mutation of T to C at the binding domain resulting in a Valine to Alanine amino acid change.

Isolation and Characterization of A HCMV Mutant That Is Resistant to The 4-oxo-DHQ's and 4-oxo-DHTP Compounds

In order to select for a 4-oxo-DHQ HCMV resistant mutant, virus (strain AD169) is serially passaged in the presence of 20 uM a 4-oxo-DHQ. Although we could readily select for HSV mutants using this procedure we failed to isolate an HCMV mutant, even when the virus is passaged at low drug concentrations (<5 uM). Comparison of the amino acid sequence of the HSV polymerase, Y-G-F-T-G-V-Q-H-G, and HCMV polymerase, Y-G-F-T-G-V-V-N-G, in the region of amino acid 823 (underlined amino acid) showed that there is a second valine at position 824 in the HCMV polymerase. In order to determine if both valines need to be changed in order to confer resistance to the 4-oxo-DHQ's, *in vitro* polymerase assays are done using mutant HCMV polymerases containing either V823A or V823A plus V824L (Table 3).

Table 3

HCMV Mutant Polymerase Exhibits Resistance to 4-oxo-DHQ*

Polymerase	Compound 1 IC_{50} (uM)
HCMV (wild)	4.6
HCMV V823A	17.2
HCMV V823A/V824L	42.9

*Generation of the valine to alanine at amino acid 823 of HCMV results in a 3.5-fold increase in resistance.

*Mutation of the amino acid from valine to alanine and amino acid 824 from valine to leucine results in an 9-fold increase in resistance, relative to wild type.

The V823A alone resulted in a 3.5-fold increase in the IC_{50} while the polymerase with the double amino acid change had nearly 10-fold increase in the IC_{50}. In order to isolate an HCMV resistant mutant marker rescue experiments are done. Plasmids containing the mutant polymerase genes are transfected into HFF cells along with wild type HCMV AD169 DNA. The resulting virus is then serially passaged in the presence of 20 uM compound 1 (see figure 1). A 4-oxo-DHQ resistant virus is isolated from marker rescue studies done with the HCMV polymerase gene containing mutations that result in the V823A, V824L amino acid changes, but not with the gene containing V823A change alone. The mutant selected with compound 1 (HCMV AD169-M1) exhibited ~7-fold increase in IC_{50} when tested in a plaque reduction assay compared to Ganciclovir and cidofovir which has a ≤ 2-fold change in sensitivity (Table 4).

Table 4

Plaque reduction assay of 4-oxo-DHQ resistant HCMV*

Drug	HCMV AD169 IC_{50} (μM)	HCMV AD169 – M1 IC_{50} (μM)
Compound 1	0.7	4.7
Ganciclovir	0.9	1.0
Cidofovir	0.3	0.6

*Recombination of wild-type HCMV with a polymerase gene containing the valine to alanine at amino acid 823 and the valine to leucine at amino acid 824 allowed for selection of resistant virus with about 7-fold less sensitivity to compound 1.

*Sensitivity of resistant HCMV virus to Ganciclovir and Cidofovir verifies that the 4-oxo-DHQ's mechanism for inhibiting the polymerase protein is unique

The entire coding region of the HCMV polymerase genes from both the parent
strain and the resistant virus are sequenced. The DNA sequencing is again done using viral
DNA as the template thus avoiding cloning of the polymerase genes. Comparison of the
DNA sequence of the two polymerase genes demonstrated that the resistant mutant
5   contained two point mutations that resulted in the predicted V823A, V824L amino acid
changes. As with the HSV resistant viruses these results demonstrate the critical role of the
region encompassing amino acid 823 for inhibition of polymerase activity by these
compounds.

10   <u>Antiviral Activity of Nucleoside and Non-Nucleoside Polymerase Inhibitors Against 4-
oxo-DHQ Resistant Mutants</u>

In order to determine if the 4-HQ binding domain mutations alter the sensitivity of
the HSV-1, HSV-2 and HCMV mutants to both non-nucleoside (4-oxo-DHQ's) and
nucleoside inhibitors (e.g Acyclovir and ganciclovir) several of the mutants are tested in
15   plaque reduction assays against a series of non-nucleoside compounds including Foscarnet
(PFA), 4-HQ's 4-oxo-DHQ's and 4-oxo-DHTP's (Table 5). The mutants are also tested
against a series of nucleoside inhibitors including acyclovir and ganciclovir (Table 5). The
activity of these compounds against the mutants is compared to their activity against the
wild type strains that are used to isolate the HSV and HCMV mutants. When tested against
20   a number of 4-HQ's, 4-oxo-DHQ's and 4-oxo-DHTP's and other related classes of
compounds all of the drugs are found to inhibit the wild type virus with IC_{50} values ranging
from <0.1 uM to 30 uM. When these drugs are tested against the resistant viruses they are
found to have IC_{50} values 5 to 10 fold higher then the parent virus. There is little if any
difference in the IC_{50} values of the nucleoside compounds and the non-nucleoside PFA
25   between the wild type and mutant HSV-1, HSV-2, and HCMV viruses. These results
demonstrate that the amino acid change in the binding domain (V823A in the HSV-1
polymerase, V826A in the HSV2-MS polymerase, V828A in the HSV2-186 polymerase,
and the V823A/V824L changes in the HCMV polymerase) resulted in resistance to the 4-
oxo-DHQ's and 4-oxo-DHTP's, which provides further evidence that these classes of
30   compounds share an affinity for a region we refer to as the binding domain. In contrast,
these amino acid changes did not alter the activity of these viruses to other classes of
polymerase inhibitors.

Table 5

Antiviral activity of nucleoside and non-nucleoside polymerase inhibitors
against HSV-1, HSV-2, and HCMV Isolates selected for 4-oxo-DHQ resistance*

	Plaque Reduction Assay – IC_{50} (μM)					
Drug	HSV-2 MS	HSV-2 MS-M1	HSV-1 KOS	HSV-1 KOS-M1	HCMV AD169	HCMV AD169-M1
6	28.8	>50	24.6	>50	5.1	>16
7	8.8	27.9	6.5	>50	0.3	3.4
8	2.3	>50	5.1	>50	<0.1	1.1
9	0.9	48.7	1.9	>50	<0.1	3.1
10	29.2	>50	15.8	>50	1.1	>16
11	3.0	>50	3.1	>50	0.7	3.9
12	0.4	12.5	1.3	>50	0.2	1.1
13	5.3	>50	5.5	<25	2.7	>16
14	1.6	>50	28.4	>50	0.9	18.4
2	1.3	>50	3.3	>50	0.4	4.0
4	2.1	28.4	4.2	>50	0.6	2.1
3	0.8	>50	4.0	>50	1.5	6.2
15	5.9	>50	>50	>50	0.7	7.7
Iudr	5.0	6.1	1.1	0.8	ND	ND
Bvdu	5.8	5.9	2.1	0.1	ND	ND
ACV	2.4	2.8	3.9	4.4	ND	ND
AraC	0.2	0.1	0.2	0.2	ND	ND
AraT	6.6	3.6	11.6	3.6	ND	ND
AraA	10.6	18.2	26.1	27.2	ND	ND
GCVir	ND	ND	ND	ND	0.8	0.8
CDV	ND	ND	ND	ND	0.4	0.3
PFA	ND	ND	ND	ND	38	<20

*HSV-2 MS, HSV-1 KOS, HCMV AD169: wild type strains
*HSV-2 MS-M1, HSV-1 KOS-M1, HCMV AD169-M1: mutants selected for 4-oxo-DHQ resistance
*ND – Not Done.

Antiviral compounds identified by the present invention can conveniently be administered in a pharmaceutical composition containing the compound in combination with a suitable excipient, the composition being useful in combating viral infections. Pharmaceutical compositions containing a compound appropriate for antiviral use are prepared by methods and contain excipients which are well known in the art. A generally recognized compendium of such methods and ingredients is Remington's Pharmaceutical Sciences by E.W. Martin (Mark Publ. Co., 15th Ed., 1975).

Antiviral compounds identified by the present invention and their compositions can be administered parenterally (for example, by intravenous, intraperitoneal or intramuscular

injection), topically, orally, or rectally, depending on whether the preparation is used to treat internal or external viral infections.

For oral therapeutic administration, the active compound may be combined with one or more excipients and used in the form of ingestible tablets, buccal tablets, troches,

5   capsules, elixirs, suspensions, syrups, wafers, and the like. Such compositions and preparations should contain at least 0.1% of active compound. The percentage of the compositions and preparations may, of course, be varied and may conveniently be between about 2 to about 60% of the weight of a given unit dosage form. The amount of active compound in such therapeutically useful compositions is such that an effective dosage level

10   will be obtained.

The tablets, troches, pills, capsules, and the like may also contain the following: . binders such as gum tragacanth, acacia, corn starch or gelatin; excipients such as dicalcium phosphate; a disintegrating agent such as corn starch, potato starch, alginic acid and the like; a lubricant such as magnesium stearate; and a sweetening agent such as sucrose,

15   fructose, lactose or aspartame or a flavoring agent such as peppermint, oil of wintergreen, or cherry flavoring may be added. When the unit dosage form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier, such as a vegetable oil or a polyethylene glycol. Various other materials may be present as coatings or to otherwise modify the physical form of the solid unit dosage form. For instance, tablets, pills, or

20   capsules may be coated with gelatin, wax, shellac or sugar and the like. A syrup or elixir may contain the active compound, sucrose or fructose as a sweetening agent, methyl and propylparabens as preservatives, a dye and flavoring such as cherry or orange flavor. Of course, any material used in preparing any unit dosage form should be pharmaceutically acceptable and substantially non-toxic in the amounts employed. In addition, the active .

25   compound may be incorporated into sustained-release preparations and devices.

Antiviral compounds identified by the present invention and their compositions can also be administered intravenously or intraperitoneally by infusion or injection. Solutions of the active compound or its salts can be prepared in water, optionally mixed with a nontoxic surfactant. Dispersions can also be prepared in glycerol, liquid polyethylene

30   glycols, triacetin, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations contain a preservative to prevent the growth of microorganisms.

Pharmaceutical dosage forms suitable for injection or infusion can include sterile aqueous solutions or dispersions or sterile powders comprising the active ingredient which

are adapted for the extemporaneous preparation of sterile injectable or infusible solutions or dispersions, optionally encapsulated in liposomes. In all cases, the ultimate dosage form should be sterile, fluid and stable under the conditions of manufacture and storage. The liquid carrier or vehicle can be a solvent or liquid dispersion medium comprising, for

5   example, water, ethanol, a polyol (for example, glycerol, propylene glycol, liquid polyethylene glycols, and the like), vegetable oils, nontoxic glyceryl esters, and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the formation of liposomes, by the maintenance of the required particle size in the case of dispersions or by the use of surfactants. The prevention of the action of microorganisms can be brought

10   about by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, buffers or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

15   Sterile injectable solutions can be prepared by incorporating the active compound in the required amount in the appropriate solvent with various of the other ingredients enumerated above, as required, followed by filter sterilization. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and the freeze drying techniques, which yield a powder of

20   the active ingredient plus any additional desired ingredient present in the previously sterile-filtered solutions.

For topical administration, the present compounds may be applied in pure form, i.e., when they are liquids. However, it will generally be desirable to administer them to the skin as compositions or formulations, in combination with a dermatologically acceptable

25   carrier, which may be a solid or a liquid.

Useful solid carriers include finely divided solids such as talc, clay, microcrystalline cellulose, silica, alumina and the like. Useful liquid carriers include water, alcohols or glycols or water-alcohol/glycol blends, in which the present compounds can be dissolved or dispersed at effective levels, optionally with the aid of non-toxic surfactants. Adjuvants

30   such as fragrances and additional antimicrobial agents can be added to optimize the properties for a given use. The resultant liquid compositions can be applied from absorbent pads, used to impregnate bandages and other dressings, or sprayed onto the affected area using pump-type or aerosol sprayers. Thickeners such as synthetic polymers, fatty acids,

fatty acid salts and esters, fatty alcohols, modified celluloses or modified mineral materials can also be employed with liquid carriers to form spreadable pastes, gels, ointments, soaps, and the like, for application directly to the skin of the user.

Examples of useful dermatological compositions which can be used to deliver the compounds of formula I to the skin are known to the art; for example, see Jacquet et al. (U.S. Pat. No. 4,608,392), Geria (U.S. Pat. No. 4,992,478), Smith et al. (U.S. Pat. No. 4,559,157) and Wortzman (U.S. Pat. No. 4,820,508).

Useful dosages of the compounds of formula I can be determined by comparing their *in vitro* activity, and *in vivo* activity in animal models. Methods for the extrapolation of effective dosages in mice, and other animals, to humans are known to the art; for example, see U.S. Pat. No. 4,938,949.

The compound is conveniently administered in unit dosage form; for example, containing 5 to 1000 mg, conveniently 10 to 750 mg, most conveniently, 50 to 500 mg of active ingredient per unit dosage form. The desired dose may conveniently be presented in a single dose or as divided doses administered at appropriate intervals, for example, as two, three, four or more sub-doses per day. The sub-dose itself may be further divided, e.g., into a number of discrete loosely spaced administrations; such as multiple inhalations from an insufflator or by application of a plurality of drops into the eye.

For internal infections, the compositions can be administered orally or parenterally at dose levels, calculated as the free base, of about 0.1 to 300 mg/kg, preferably 1.0 to 30 mg/kg of mammal body weight, and can be used in man in a unit dosage form, administered one to four times daily in the amount of 1 to 1000 mg per unit dose.

For parenteral administration or for administration as drops, as for eye infections, the compounds are presented in aqueous solution in a concentration of from about 0.1 to about 10%, more preferably about 0.1 to about 7%. The solution may contain other ingredients, such as emulsifiers, antioxidants or buffers.

Generally, the concentration of the compound(s) of formula I in a liquid composition, such as a lotion, will be from about 0.1-25 wt-%, preferably from about 0.5-10 wt-%. The concentration in a semi-solid or solid composition such as a gel or a powder will be about 0.1-5 wt-%, preferably about 0.5-2.5 wt-%.

The exact regimen for administration of the compounds and compositions disclosed herein will necessarily be dependent upon the needs of the individual subject being treated, the type of treatment and, of course, the judgment of the attending practitioner.

The antiviral activity of a compound of the invention can be determined using pharmacological models which are well known to the art, or using Test A described below.

The compounds of formula (I) and pharmaceutically acceptable salts thereof are useful as antiviral agents. Thus, they are useful to combat viral infections in animals,

5   including man. The compounds are generally active against herpes viruses, and are particularly useful against the varicella zoster virus, the Epstein-Barr virus, the herpes simplex virus, the human herpes virus type 8 (HHV-8) and the cytomegalovirus (CMV).

10

CLAIMS

We claim:

1.   A method of selecting compounds that inhibit herpes viruses comprising:

a)   measuring IC_{50} of a compound of interest that inhibits a wild type herpes virus,

5   b)   measuring IC_{50} of the same compound that inhibits a binding domain mutant herpes virus which is the same strain as the wild type herpes virus,

c)   comparing IC_{50} of step a with IC_{50} of step b; and

d)   selecting the compound of interest wherein the IC_{50} of step b is at least 3 times greater than the IC_{50} of step a.

10

2.   A method of selecting compounds that inhibit herpes viruses comprising:

a)   measuring IC_{50} of a compound of interest that inhibits a binding domain mutant herpes virus,

b)   measuring IC_{50} of the same compound that inhibits a wild type herpes virus which is

15   the same strain as the mutant herpes virus,

c)   comparing IC_{50} of step a with IC_{50} of step b; and

d)   selecting the compound of interest wherein the IC_{50} of step a is at least 3 times greater than the IC_{50} of step b.

20   3.   The method of claim 1 or 2 wherein the herpes virus is HSV-1, HSV-2, HCMV, VZV, EBV, or HHV-8.

4.   A method of selecting compounds that inhibit herpes viruses comprising:

a)   measuring IC_{50} of a compound of interest that inhibits a wild type HSV-1,

25   b)   measuring IC_{50} of the same compound that inhibits a binding domain mutant HSV-1 which is the same strain as the wild type herpes virus,

c)   comparing IC_{50} of step a with IC_{50} of step b; and

d)   selecting the compound of interest wherein the IC_{50} of step b is at least 3 times greater than the IC_{50} of step a.

30

5.   A method of selecting compounds that inhibit herpes viruses comprising:

a)   measuring IC_{50} of a compound of interest that inhibits a binding domain mutant HSV-1,

b)   measuring IC_{50} of the same compound that inhibits a wild type herpes virus which is the same strain as the mutant HSV-1,

c)   comparing IC_{50} of step a with IC_{50} of step b; and

d)   selecting the compound of interest wherein the IC_{50} of step a is at least 3 times

5   greater than the IC_{50} of step b.

6.   The method of claim 4 or 5 wherein HSV-1 is HSV-1 KOS, HSV-1 F, HSV-1 DJL or HSV-1 Patton.

10   7.   The method of claim 5 or 6 wherein the mutation of a wild type herpes virus to mutant herpes virus is at amino acid 823 from valine to alanine.

8.   A method of selecting compounds that inhibit herpes viruses comprising:

a)   measuring IC_{50} of a compound of interest that inhibits a wild type HSV-2,

15   b)   measuring IC_{50} of the same compound that inhibits a binding domain mutant HSV-2 which is the same strain as the wild type herpes virus,

c)   comparing IC_{50} of step a with IC_{50} of step b; and

d)   selecting the compound of interest wherein the IC_{50} of step b is at least 3 times greater than the IC_{50} of step a.

20

9.   A method of selecting compounds that inhibit herpes viruses comprising:

a)   measuring IC_{50} of a compound of interest that inhibits a binding domain mutant HSV-2,

b)   measuring IC_{50} of the same compound that inhibits a wild type herpes virus which is

25   the same strain as the mutant HSV-2,

c)   comparing IC_{50} of step a with IC_{50} of step b; and

d)   selecting the compound of interest wherein the IC_{50} of step a is at least 3 times greater than the IC_{50} of step b.

30   10.   The method of claim 8 or 9 wherein HSV-2 is HSV-2 MS, HSV-2 35D, or HSV-2 186.

11.   A method of selecting compounds that inhibit herpes viruses comprising:

a) measuring IC_{50} of a compound of interest that inhibits a wild type HCMV,

b) measuring IC_{50} of the same compound that inhibits a binding domain mutant HCMV which is the same strain as the wild type herpes virus,

c) comparing IC_{50} of step a with IC_{50} of step b; and

5   d) selecting the compound of interest wherein the IC_{50} of step b is at least 3 times greater than the IC_{50} of step a.

12. A method of selecting compounds that inhibit herpes viruses comprising:

a) measuring IC_{50} of a compound of interest that inhibits a binding domain mutant

10   HCMV,

b) measuring IC_{50} of the same compound that inhibits a wild type herpes virus which is the same strain of the mutant HCMV,

c) comparing IC_{50} of step a with IC_{50} of step b; and

d) selecting the compound of interest wherein the IC_{50} of step a is at least 3 times

15   greater than the IC_{50} of step b.

13. The method of claim 8 or 9 wherein HCMV is AD169.

14. The methods of claims 1, 4, 8, or 11 wherein IC_{50} of step b is at least 5 times greater

20   than the IC_{50} of step a.

15. The methods of claims 2, 5, 9, or 12 wherein IC_{50} of step a is at least 5 times greater than the IC_{50} of step b.

25   16. A use of compounds for manufacturing of medicinals for selectively treating diseases caused by herpes viruses in a human host comprising administering a compound to a human in need of such treatment wherein said compound inhibits herpes viruses by interaction with the binding domain in the viral DNA polymerase.

30   17. A use of compounds for manufacturing of medicinals for selectively inhibiting herpes viruses in a human host comprising administering a compound to a human in need of such treatment wherein IC_{50} of the compound that inhibits a binding domain

mutant herpes virus is at lease 3 times greater than IC_{50} of the compound that inhibits a wild type herpes virus which is the same strain as the mutant herpes virus.

18.   The use of claim 17 wherein IC_{50} of the compound that inhibits a binding domain mutant herpes virus is at lease 5 times greater than IC_{50} of the compound that inhibits a wild type herpes virus which is the same strain as the mutant herpes viruse.

19.   The use of claim 17 wherein herpes viruses is HSV-1, HSV-2, HCMV, VZV, EBV, or HHV-8.

20.   A use of compounds for manufacturing of medicinals for treating herpesviral infections in a human host wherein IC_{50} of the compound that inhibits a binding domain mutant herpes virus is at lease 5 times greater than IC_{50} of the compound that inhibits a wild type herpes virus which is the same strain as the mutant herpes virus.

21.   A use of compounds for manufacturing of medicinals for treating herpesviral infections in a human host wherein said compound inhibits the herpesvirus by interacting with the binding domain in the viral DNA polymerase.

22.   The herpesviral infection of claim 20 or 21 which is HSV-1, HSV-2, HCMV, VZV, EBV, or HHV-8 infection.

23.   A compound for the inhibiting of herpesvirus DNA polymerases wherein passage of a wild type herpes virus in the presence of said compound results a change of the wild type HSV-1 polymerases at amino acid 823 from valine to alanine.

24.   A compound for inhibiting herpesvirus DNA polymerases wherein passage of a wild type herpes virus in the presence of said compound results in a change of the wild type HCMV polymerases at amino acid 823 from valine to alanine and at amino acid 824 from valine to leuline.

25.   A mutant herpesvirus DNA molecule having a nucleotide sequence selected from a group consisting of SEQ.ID.NO. 1; SEQ.ID.NO. 3; SEQ.ID.NO. 5; SEQ.ID.NO. 7; SEQ.ID.NO. 9; and SEQ.ID.NO. 11.

5   26.   A mutant herpesvirus polymerase amino acid molecule having an amino acid sequence selected from a group consisting of SEQ.ID.NO. 2; SEQ.ID.NO. 4; SEQ.ID.NO. 6; SEQ.ID.NO. 8; SEQ.ID.NO. 10 and SEQ.ID.NO. 12.

10

Figure 1   **4-HQ, 4-oxo-DHQ and 4-oxo-DHTP antiviral compounds**
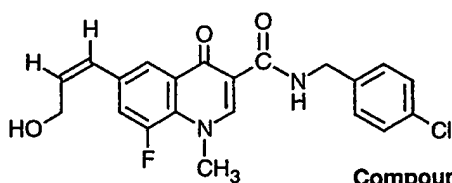
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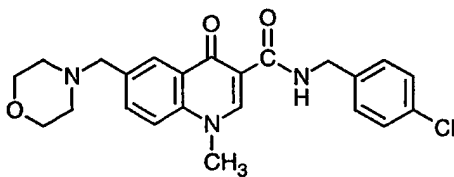
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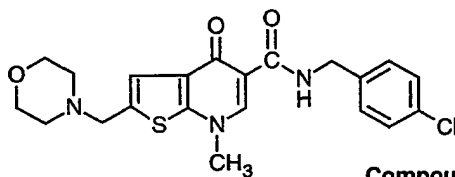
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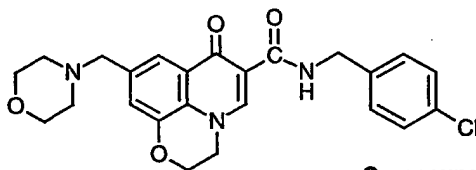
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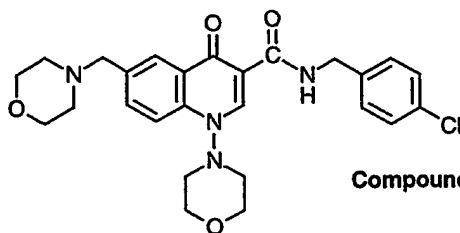
Compound No. 5

(Figure 1 continue)
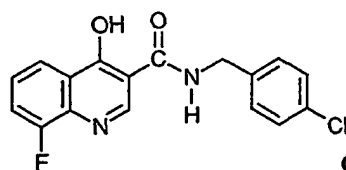
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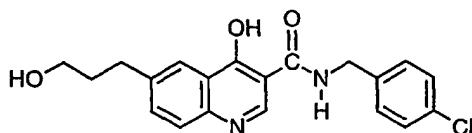
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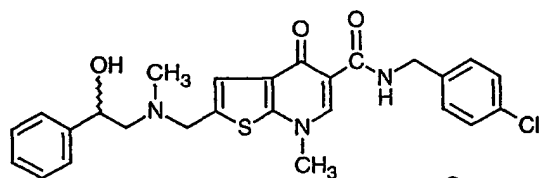
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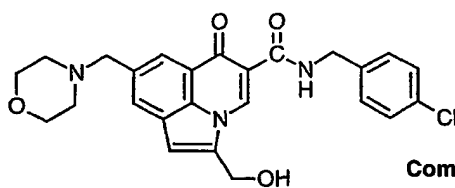
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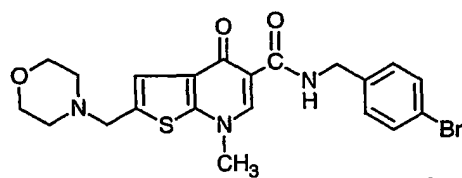
Compound No. 10

(Figure 1 continue)

Compound No. 11

Compound No. 12

Compound No. 13
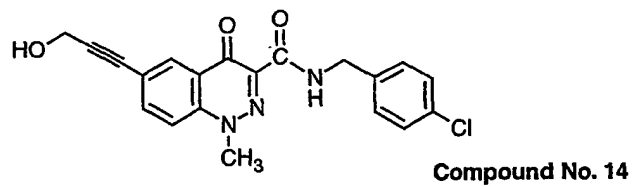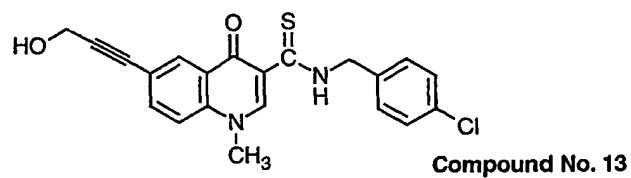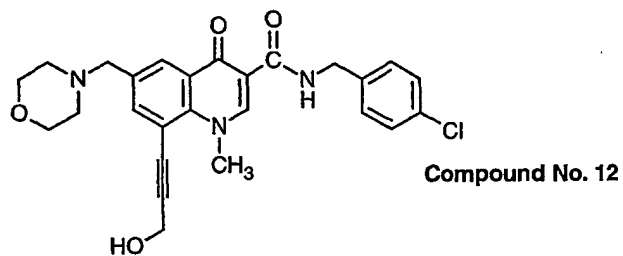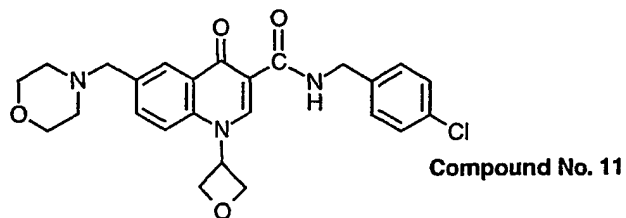
Compound No. 14

(Figure 1 continue)
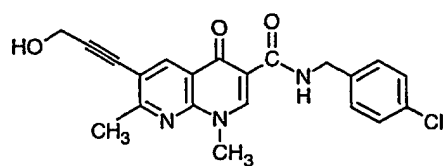
Compound No.15
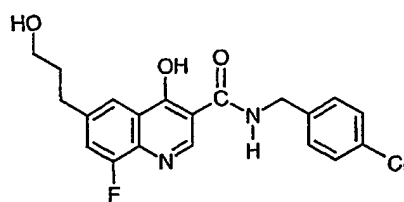
Compound 17

Figure 2. The HSV1 (KOS Strain) DNA Polymerase Amino Acid 823 is Critical for Resistance to 4-Hydroxyquinolines and Related Compounds

HSV1-KOS-M1	Y	G	F	T	G	A	Q	H	G - 826
HSV1	Y	G	F	T	G	V	Q	H	G - 826
HSV2	Y	G	F	T	G	V	Q	H	G - 829
VZV	Y	G	F	T	G	V	A	Q	G - 791
EBV	Y	G	F	T	G	V	A	N	G - 696
HCMV	Y	G	F	T	G	V	V	N	G - 826
HHV6	Y	G	V	T	G	A	A	H	G - 681
HHV7	Y	G	V	T	G	A	T	H	S - 681
HHV8	Y	G	F	T	G	V	A	S	G - 696
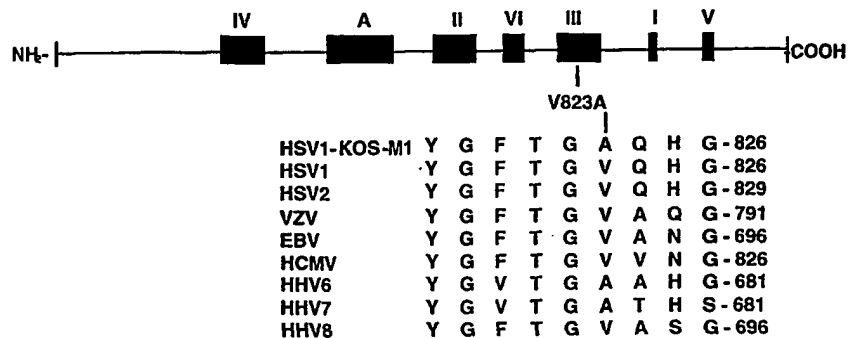
Schematic of HSV1 polymerase illustrating the conserved regions A and I-VI found in class 2 polymerases. Also shown are the amino acid sequence for the highly conserved herpesvirus domain in region III which surrounds the HSV1 amino acid 823.

5

Figure 3   **Serial Passage of HSV-1 in Presence of 20 μM compound 17**
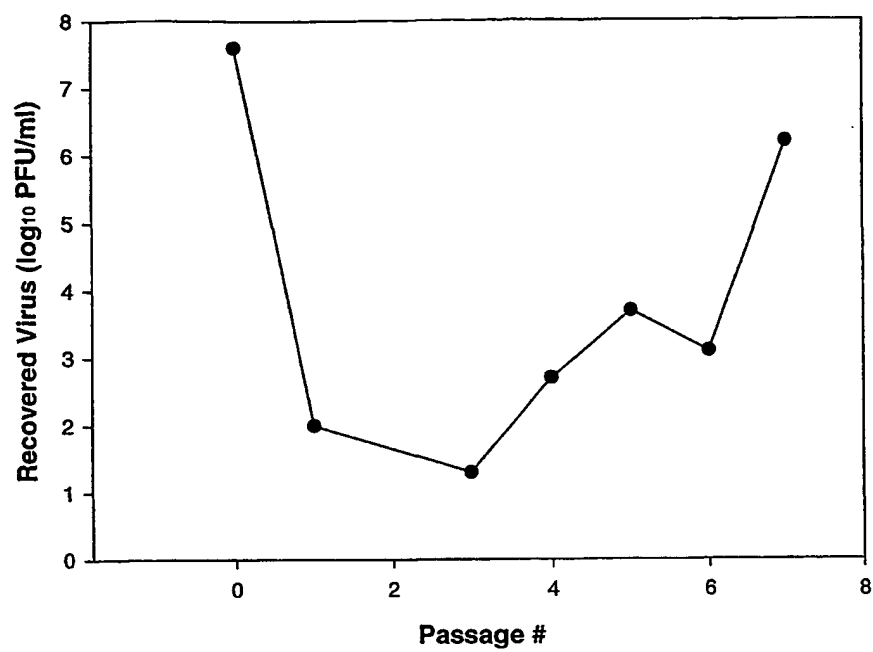
Figure 4   Comparison of Wild type HSV-1 and HSV-2 DNA Polymerases Amino

Acid Sequences Aligned by Amino Acid Homology*

```
      HSV2-MS      MFCAAGGPTS PGGKSAARAA SGFFAPHNPR GATQTAPPPC RRQNFYNPHL -50
      HSV2-186     MFCAAGGPAS PGGKSAARAA SGFFAPHNPR GATQTAPPPC RRQNFYNPHL -50
   5  HSV1-Kos     MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGR.GPPPC LRQNFYNPYL -49
      HSV1-Patton  MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGR.GPPPC LRQNFYNPYL -49
      HSV1-DJL     MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGR.GPPPC LRQNFYNPYL -49
      HSV1-F       MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGR.GPPPC LRQNFYNPYL -49


  10  HSV2-MS      AQTGTQPKAP GPAQRHTYYS ECDEFRFIAP RSLDEDAPAE QRTGVHDGRL -100
      HSV2-186     AQTGTQPKAP GPAQRHTYYS ECDEFRFIAP RSLDEDAPAE QRTGVHDGRL -100
      HSV1-Kos     APVGTQQKPT GPTQRHTYYS ECDEFRFIAP RVLDEDAPPE KRAGVHDGHL -99
      HSV1-Patton  APVGTQQKPT GPTQRHTYYS ECDEFRFIAP RVLDEDAPPE KRAGVHDGHL -99
      HSV1-DJ1     APVGTQQKPT GPTQRHTYYS ECDEFRFIAP RVLDEDAPPE KRAGVHDGHL -99
  15  HSV1-F       APVGTQQKPT GPTQRHTYYS ECDEFRFIAP RVLDEDAPPE KRAGVHDGHL -99


      HSV2-MS      RRAPKVYCGG DERDVLRVGP EGFWPRRLRL WGGADHAPKG FDPTVTVFHV -150
      HSV2-186     RRAPKVYCGG DERDVLRVGP EGFWPRRLRL WGGADHAPEG FDPTVTVFHV -150
      HSV-Kos      KRAPKVYCGG DERDVLRVGS GGFWPRRSRL WGGVDHAPAG FNPTVTVFHV -149
  20  HSV1-Patton  KRAPKVYCGG DERDVLRVGS GGFWPRRSRL WGGVDHAPAG FNPTVTVFHV -149
      HSV1-DJL     KRAPKVYCGG DERDVLRVGS GGFWPRRSRL WGGVDHAPAG FNPTVTVFHV -149
      HSV1-F       KRAPKVYCGG DERDVLRVGS GGFWPRRSRL WGGVDHAPAG FNPTVTVFHV -149


      HSV2-MS      YDILEHVEHA YSMRAAQLHE RFMDAITPAG TVITLLGLTP EGHRVAVHVY -200
  25  HSV2-186     YDILEHVEHA YSMRAAQLHE RFMDAITPAG TVITLLGLTP EGHRVAVHVY -200
      HSV-Kos      YDILENVEHA YGMRAAQFHA RFMDAITPTG TVITLLGLTP EGHRVAVHVY -199
      HSV1-Patton  YDILENVEHA YGMRAAQFHA RFMDAITPTG TVITLLGLTP EGHRVAVHVY -199
      HSV1-DJL     YDILENVEHA YGMRAAQFHA RFMDAITPTG TVITLLGLTP EGHRVAVHVY -199
      HSV1-F       YDILENVEHA YGMRAAQFHA RFMDAITPTG TVITLLGLTP EGHRVAVHVY -199
  30
      HSV2-MS      GTRQYFYMNK AEVDRHLQCR APRDLCERLA AALRESPGAS FRGISADHFE -250
      HSV2-186     GTRQYFYMNK AEVDRHLQCR APRDLCERLA AALRESPGAS FRGISADHFE -250
      HSV-Kos      GTRQYFYMNK EEVDRHLQCR APRDLCERMA AALRESPGAS FRGISADHFE -249
      HSV1-Patton  GTRQYFYMNK EEVDRHLQCR APRDLCERMA AALRESPGAS FRGISADHFE -249
  35  HSV1-DJL     GTRQYFYMNK EEVDRHLQCR APRDLCERMA AALRESPGAS FRGISADHFE -249
      HSV1-F       GTRQYFYMNK EEVDRHLQCR APRDLCERMA AALRESPGAS FRGISADHFE -249


      HSV2-MS      AEVVERADVY YYETRPTLYY RVFVRSGRAL AYLCDNFCPA IRKYEGGVDA -300
      HSV2-186     AEVVERADVY YYETRPTLYY RVFVRSGRAL AYLCDNFCPA IRKYEGGVDA -300
  40  HSV-Kos      AEVVERTDVY YYETRPALFY RVYVRSGRVL SYLCDNFCPA IKKYEGGVDA  -299
      HSV1-Patton  AEVVERTDVY YYETRPALFY RVYVRSGRVL SYLCDNFCPA IKKYEGGVDA -299
      HSV1-DJL     AEVVERTDVY YYETRPALFY RVYVRSGRVL SYLCDNFCPA IKKYEGGVDA -299
      HSV1-F       AEVVERTDVY YYETRPALFY RVYVRSGRVL SYLCDNFCPA IKKYEGGVDA -299


  45  HSV2-MS      TTRFILDNPG FVTFGWYRLK PGRGNAPAQP RPPTAFGTSS DVEFNCTADN -350
      HSV2-186     TTRFILDNPG FVTFGWYRLK PGRGNAPAQP RPPTAFGTSS DVEFNCTADN -350
      HSV-Kos      TTRFILDNPG FVTFGWYRLK PGRNNTLAQP RAPMAFGTSS DVEFNCTADN -349
      HSV1-Patton  TTRFILDNPG FVTFGWYRLK PGRNNTLAQP RAPMAFGTSS DVEFNCTADN -349
      HSV1-DJL     TTRFILDNPG FVTFGWYRLK PGRNNTLAQP RAPMAFGTSS DVEFNCTADN -349
  50  HSV1-F       TTRFILDNPG FVTFGWYRLK PGRNNTLAQP RAPMAFGTSS DVEFNCTADN -349


      HSV2-MS      LAVEGAMCDL PAYKLMCFDI ECKAGGEDEL AFPVAERPED LVIQISCLLY -400
      HSV2-186     LAVEGAMCDL PAYKLMCFDI ECKAGGEDEL AFPVAERPED LVIQISCLLY -400
      HSV-Kos      LAIEGGMSDL PAYKLMCFDI ECKAGGEDEL AFPVAGHPED LVIQISCLLY -399
  55  HSV1-Patton  LAIEGGMSDL PAYKLMCFDI ECKAGGEDEL AFPVAGHPED LVIQISCLLY -399
      HSV1-DJL     LAIEGGMSDL PAYKLMCFDI ECKAGGEDEL AFPVAGHPED LVIQISCLLY -399
      HSV1-F       LAIEGGMSDL PAYKLMCFDI ECKAGGEDEL AFPVAGHPED LVIQISCLLY -399


      HSV2-MS      DLSTTALEHI LLFSLGSCDL PESHLSDLAS RGLPAPVVLE FDSEFEMLLA -450
  60  HSV2-186     DLSTTALEHI LLFSLGSCDL PESHLSDLAS RGLPAPVVLE FDSEFEMLLA -450
      HSV-Kos      DLSTTALEHV LLFSLGSCDL PESHLNELAA RGLPTPVVLE FDSEFEMLLA -449
      HSV1-Patton  DLSTTALEHV LLFSLGSCDL PESHLNELAA RGLPTPVVLE FDSEFEMLLA -449
      HSV1-DJL     DLSTTALEHV LLFSLGSCDL PESHLNELAA RGLPTPVVLE FDSEFEMLLA -449
      HSV1-F       DLSTTALEHV LLFSLGSCDL PESHLNELAA RGLPTPVVLE FDSEFEMLLA -449
  65
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      HSV2-MS      FMTFVKQYGP EFVTGYNIIN FDWPFVLTKL TEIYKVPLDG YGRMNGRGVF -500
      HSV2-186     FMTFVKQYGP EFVTGYNIIN FDWPFVLTKL TEIYKVPLDG YGRMNGRGVF -500
      HSV-Kos      FMTLVKQYGP EFVTGYNIIN FDWPFLLAKL TDIYKVPLDG YGRMNGRGVF -499
      HSV1-Patton  FMTLVKQYGP EFVTGYNIIN FDWPFLLAKL TDIYKVPLDG YGRMNGRGVF ₸499
 5    HSV1-DJL     FMTLVKQYGP EFVTGYNIIN FDWPFLLAKL TDIYKVPLDG YGRMNGRGVF -499
      HSV1-F       FMTLVKQYGP EFVTGYNIIN FDWPFLLAKL TDIYKVPLDG YGRMNGRGVF -499


      HSV2-MS      RVWDIGQSHF QKRSKIKVNG MVNIDMYGII TDKVKLSSYK LNAVAEAVLK -550
      HSV2-186     RVWDIGQSHF QKRSKIKVNG MVNIDMYGII TDKVKLSSYK LNAVAEAVLK -550
10    HSV-Kos      RVWDIGQSHF QKRSKIKVNG MVNIDMYGII TDKIKLSSYK LNAVAEAVLK -549
      HSV1-Patton  RVWDIGQSHF QKRSKIKVNG MVNIDMYGII TDKIKLSSYK LNAVAEAVLK -549
      HSV1-DJL     RVWDIGQSHF QKRSKIKVNG MVNIDMYGII TDKIKLSSYK LNAVAEAVLK -549
      HSV1-F       RVWDIGQSHF QKRSKIKVNG MVNIDMYGII TDKIKLSSYK LNAVAEAVLK -549


15    HSV2-MS      DKKKDLSYRD IPAYYASGPA QRGVIGEYCV QDSLLVGQLF FKFLPHLELS -600
      HSV2-186     DKKKDLSYRD IPAYYASGPA QRGVIGEYCV QDSLLVGQLF FKFLPHLELS -600
      HSV-Kos      DKKKDLSYRD IPAYYAAGPA QRGVIGEYCI QDSLLVGQLF FKFLPHLELS -599
      HSV1-Patton  DKKKDLSYRD IPAYYAAGPA QRGVIGEYCI QDSLLVGQLF FKFLPHLELS -599
      HSV1-DJL     DKKKDLSYRD IPTYYAAGPA QRGVIGEYCI QDSLLVGQLF FKFLPHLELS -599
20    HSV1-F       DKKKDLSYRD IPAYYAAGPA QRGVIGEYCI QDSLLVGQLF FKFLPHLELS -599


      HSV2-MS      AVARLAGINI TRTIYDGQQI RVFTCLLRLA GQKGFILPDT QGRFRGLDKE -650
      HSV2-186     AVARLAGINI TRTIYDGQQI RVFTCLLRLA GQKGFILPDT QGRFRGLDKE -650
      HSV-Kos      AVARLAGINI TRTIYDGQQI RVFTCLLRLA DQKGFILPDT QGRFRGAGGE -649
25    HSV1-Patton  AVARLAGINI TRTIYDGQQI RVFTCLLRLA DQKGFILPDT QGRFRGAGGE -649
      HSV1-DJL     AVARLAGINI TRTIYDGQQI RVFTCLLRLA DQKGFILPDT QGRFRGAGGE -649
      HSV1-F       AVARLAGINI TRTIYDGQQI RVFTCLLRLA DQKGFILPDT QGRFRGGGGE -649


      HSV2-MS      APKRPAVPRG EGERPGDGNG DEDKDDDE.. DEDGDERE.E VARETGGRHV -697
30    HSV2-186     APKRPAVPRG EGERPGDGNG DEDKDDDEDG DEDGDERE.E VARETGGRHV -697
      HSV-Kos      APKRPAAARE DEERP..... EEEGEDEDER EEGGGEREPE GARETAGRHV -694
      HSV1-Patton  APKRPAAARE DEERP..... EEEGEDEDER EEGGGEREPE GARETAGRHV -694
      HSV1-DJL     APKRPAAARE DEERP..... EEEGEDENER EEGGGEREPE GARETAGRHV -694
      HSV1-F       APKRPAAARE DEERP..... EEEGEDEDER EEGGGEREPE GARETAGRHV -694
35
      HSV2-MS      GYQGARVLDP TSGFHVDPVV VFDFASLYPS IIQAHNLCFS TLSLRPEAVA -747
      HSV2-186     GYQGARVLDP TSGFHVDPVV VFDFASLYPS IIQAHNLCFS TLSLRPEAVA -749
      HSV-Kos      GYQGARVLDP TSGFHVNPVV VFDFASLYPS IIQAHNLCFS TLSLRADAVA -744
      HSV1-Patton  GYQGARVLDP ISGFHVNPVV VFDFASLYPS IIQAHNLCFS TLSLRADAVA -744
40    HSV1-DJL     GYQGARVLDP TSGFHVNPVV VFDFASLYPS IIQAHNLCFS TLSLRADAVA -744
      HSV1-F       GYQGARVLDP TSGFHVNPVV VFDFASLYPS IIQAHNLCFS TLSLRADAVA -744


      HSV2-MS      HLEADRDYLE IEVGGRRLFF VKAHVRESLL SILLRDWLAM RKQIRSRIPQ -797
      HSV2-186     HLEADRDYLE IEVGGRRLFF VKAHVRESLL SILLRDWLAM RKQIRSRIPQ -799
45    HSV-Kos      HLEAGKDYLE IEVGGRRLFF VKAHVRESLL SILLRDWLAM RKQIRSRIPQ -794
      HSV1-Patton  HLEAGKDYLE IEVGGRRLFF VKAHVRESLL SILLRDWLAM RKQIRSRIPQ -794
      HSV1-DJL     HLEAGKDYLE IEVGGRRLFF VKAHVRESLL SILLRDWLAM RKQIRSRIPQ -794
      HSV1-F       HLEAGKDYLE IEVGGRRLFF VKAHVRESLL SILLRDWLAM RKQIRSRIPQ -794


50    HSV2-MS      STPEEAVLLD KQQAAIKVVC NSVYGFTGVQ HGLLPCLHVA ATVTTIGREM -847
      HSV2-186     SPPEEAVLLD KQQAAIKVVC NSVYGFTGVQ HGLLPCLHVA ATVTTIGREM -849
      HSV-Kos      SSPEEAVLLD KQQAAIKVVC NSVYGFTGVQ HGLLPCLHVA ATVTTIGREM -844
      HSV1-Patton  SSPEEAVLLD KQQAAIKVVC NSVYGFTGVQ HGLLPCLHVA ATVTTIGREM -844
      HSV1-DJL     SSPEEAVLLD KQQAAIKVVC NSVYGFTGVQ HGLLPCLHVA ATVTTIGREM -844
55    HSV1-F       SSPEEAVLLD KQQAAIKVVC NSVYGFTGVQ HGLLPCLHVA ATVTTIGREM -844


      HSV2-MS      LLATRAYVHA RWAEFDQLLA DFPEAAGMRA PGPYSMRIIY GDTDSIFVLC -897
      HSV2-186     LLATRAYVHA RWAEFDQLLA DFPEAAGMRA PGPYSMRIIY GDTDSIFVLC -899
      HSV-Kos      LLATREYVHA RWAAFEQLLA DFPEAADMRA PGPYSMRIIY GDTDSIFVLC -894
60    HSV1-Patton  LLATREYVHA RWAAFEQLLA DFPEAADMRA PGPYSMRIIY GDTDSIFVLC -894
      HSV1-DJL     LLATREYVHA RWAAFEQLLA DFPEAADMRA PGPYSMRIIY GDTDSIFVLC -894
      HSV1-F       LLATREYVHA RWAAFEQLLA DFPEAADMRA PGPYSMRIIY GDTDSIFVLC -894


      HSV2-MS      RGLTAAGLVA MGDKMASHIS RALFLPPIKL ECEKTFTKLL LIAKKKYIGV -947
65    HSV2-186     RGLTAAGLVA MGDKMASHIS RALFLPPIKL ECEKTFTKLL LIAKKKYIGV -949
      HSV-Kos      RGLTAAGLTA MGDKMASHIS RALFLPPIKL ECEKTFTKLL LIAKKKYIGV -944
      HSV1-Patton  RGLTAAGLTA MGDKMASHIS RALFLPPIKL ECEKTFTKLL LIAKKKYIGV -944
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        HSV1-DJL      RGLTAAGLTA VGDKMASHIS RALFLPPIKL ECEKTFTKLL LIAKKKYIGV -944
        HSV1-F        RGLTAAGLTA VGDKMASHIS RALFLSPIKL ECEKTFTKLL LIAKKKYIGV -944

        HSV2-MS       ICGGKMLIKG VDLVRKNNCA FINRTSRALV DLLFYDDTVS GAAAALAERP ≠997
   5    HSV2-186      ICGGKMLIKG VDLVRKNNCA FINRTSRALV DLLFYDDTVS GAAAALAERP -999
        HSV-Kos       IYGGKMLIKG VDLVRKNNCA FINRTSRALV DLLFYDDTVS GAAAALAERP -994
        HSV1-Patton   IYGGKMLIKG VDLVRKNNCA FINRTSRALV DLLFYDDTVS GAAAALAERP -994
        HSV1-DJL      IYGGKMLIKG VDLVRKNNCA FINRTSRALV DLLFYDDTVS GAAAALAERP -994
        HSV1-F        IYGGKMLIKG VDLVRKNNCA FINRTSRALV DLLFYDDTVS GAAAALAERP -994
  10
        HSV2-MS       AEEWLARPLP EGLQAFGAVL VDAHRRITDP ERDIQDFVLT AELSRHPRAY -1047
        HSV2-186      AEEWLARPLP EGLQAFGAVL VDAHRRITDP ERDIQDFVLT AELSRHPRAY -1049
        HSV-Kos       AEEWLARPLP EGLQAFGAVL VDAHRRITDP ERDIQDFVLT AELSRHPRAY -1044
        HSV1-Patton   AEEWLARPLP EGLQAFGAVL VDAHRRITDP ERDIQDFVLT AELSRHPRAY -1044
  15    HSV1-DJL      AEEWLARPLP EGLQAFGAVL VDAHRRITDP ERDIQDFVLT AELSRHPRAY -1044
        HSV1-F        AEEWLARPLP EGLQAFGAVL VDAHRRITDP ERDIQDFVLT AELSRHPRAY -1044

        HSV2-MS       TNKRLAHLTV YYKLMARRAQ VPSIKDRIPY VIVAQTREVE ETVARLAALR -1097
        HSV2-186      TNKRLAHLTV YYKLMARRAQ VPSIKDRIPY VIVAQTREVE ETVARLAALR -1099
  20    HSV-Kos       TNKRLAHLTV YYKLMARRAQ VPSIKDRIPY VIVAQTREVE ETVARLAALR -1094
        HSV1-Patton   TNKRLAHLTV YYKLMARRAQ VPSIKDRIPY VIVAQTREVE ETVARLAALR -1094
        HSV1-DJL      TNKRLAHLTV YYKLMARRAQ VPSIKDRIPY VIVAQTREVE ETVARLAALR -1094
        HSV1-F        TNKRLAHLTV YYKLMARRAQ VPSIKDRIPY VIVAQTREVE ETVARLAALR -1094

  25    HSV2-MS       ELDAAAPGDE PAPPAALPSP AKRPRETPSH ADPPGGASKP RKLLVSELAE -1147
        HSV2-186      ELDAAAPGDE PAPPAALPSP AKRPRETPSH ADPPGGASKP RKLLVSELAE -1149
        HSV-Kos       ELDAAAPGDE PAPPAALPSP AKRPRETPSH ADPPGGASKP RKLLVSELAE -1144
        HSV1-Patton   ELDAAAPGDE PAPPAALPSP AKRPRETPSP ADPPGGASKP RKLLVSELAE -1144
        HSV1-DJL      ELDAAAPGDE PAPPAALPSP AKRPRETPSP ADPPGGASKP RKLLVSELAE -1144
  30    HSV1-F        ELDAAAPGDE PAPPAALPSP AKRPRETPLH ADPPGGASKP RKLLVSELAE -1144

        HSV2-MS       DPGYAIARGV PLNTDYYFSH LLGAACVTFK ALFGNNAKIT ESLLKRFIPE -1197
        HSV2-186      DPGYAIARGV PLNTDYYFSH LLGAACVTFK ALFGNNAKIT ESLLKRFIPE -1199
        HSV-Kos       DPAYAIAHGV ALNTDYYFSH LLGAACVTFK ALFGNNAKIT ESLLKRFIPE -1194
  35    HSV1-Patton   DPAYAIAHGV ALNTDYYFSH LLGAACVTFK ALFGNNAKIT ESLLKRFIPE -1194
        HSV1-DJL      DPAYAIAHGV ALNTDYYFSH LLGAACVTFK ALFGNNAKIT ESLLKRFIPE -1194
        HSV1-F        DPAYAIAHGV ALNTDYYFSH LLGAACVTFK ALFGNNAKIT ESLLKRFIPE -1194

        HSV2-MS       TWHPPDDVAA RLRAAGFGPA GAGATAEETR RMLHRAFDTL A* -1238
  40    HSV2-186      TWHPPDDVAA RLRAAGFGPA GAGATAEETR RMLHRAFDTL A* -1240
        HSV-Kos       VWHPPDDVAA RLRAAGFGAV GAGATAEETR RMLHRAFDTL A* -1235
        HSV1-Patton   VWHPPDDVTA RLRAAGFGAV GAGATAEETR RMLHRAFDTL A* -1235
        HSV1-DJL      VWHPPDDVAA RLRTAGFGAV GAGATAEETR RMLHRAFDTL A* -1235
        HSV1-F        VWHPPDDVAA RLRAAGFGAV GAGATAEETR RMLHRAFDTL A* -1235
  45
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*Amino acid alignment demonstrates difference in amino acid's sequences.

*The gaps "....." indicate missing amino acids relative to other stanins.

*Wild HSV2-MS is listed as SEQ. ID NO 14.

*Wild HSV2-186 is listed as SEQ. ID NO 15.

50   *Wild HSV-Kos is listed as SEQ. ID NO 16.

*Wild HSV1-Patton is listed as SEQ. ID NO 17.

*Wild HSV1-DJL is listed as SEQ. ID NO 18.

*Wild HSV1-F is listed as SEQ. ID NO 19.

55

Figure 5   DNA and amino acid sequence list

SEQ. ID. NO. 1   DNA sequence of DNA polymerase gene for HSV2-MS-M1

5   1 ATGTTTTGTG CCGCGGGCGG CCCGACTTCC CCCGGGGGGA AGTCGGCGGC

51 TCGGGCGGCG TCTGGGTTTT TTGCCCCCCA CAACCCCCGG GGAGCCACCC

101 AGACGGCACC GCCGCCTTGC CGCCGGCAGA ACTTCTACAA CCCCCACCTC

10

151 GCTCAGACCG GAACGCAGCC AAAGGCCCCC GGGCCGGCTC AGCGCCATAC

201 GTACTACAGC GAGTGCGACG AATTTCGATT TATCGCCCCG CGTTCGCTGG

15   251 ACGAGGACGC CCCCGCGGAG CAGCGCACCG GGGTCCACGA CGGCCGCCTC

301 CGGCGCGCCC CTAAGGTGTA CTGCGGGGGG GACGAGCGCG ACGTCCTCCG

351 CGTGGGCCCG GAGGGCTTCT GGCCGCGTCG CTTGCGCCTG TGGGGCGGTG

20

401 CGGACCATGC CCCCAAGGGG TTCGACCCCA CCGTCACCGT CTTCCACGTG

451 TACGACATCC TGGAGCACGT GGAACACGCG TACAGCATGC GCGCCGCCCA

25   501 GCTCCACGAG CGATTTATGG ACGCCATCAC GCCCGCCGGG ACCGTCATCA

551 CGCTTCTGGG TCTGACCCCC GAAGGCCATC GCGTCGCCGT TCACGTCTAC

601 GGCACGCGGC AGTACTTTTA CATGAACAAG GCGGAGGTGG ATCGGCACCT

30

651 GCAGTGCCGT GCCCCGCGCG ATCTCTGCGA GCGCCTGGCG GCGGCCCTGC

701 GCGAGTCGCC GGGGGCGTCG TTCCGCGGCA TCTCCGCGGA CCACTTCGAG

751 GCGGAGGTGG TGGAGCGCGC CGACGTGTAC TATTACGAAA CGCGCCCGAC

35

801 CCTGTACTAC CGCGTCTTCG TGCGAAGCGG CGCGCGCTG GCCTACCTGT

851 GCGACAACTT TTGCCCCGCG ATCAGGAAGT ACGAGGGGGG CGTCGACGCC

40

901 ACCACCCGGT TTATCCTGGA CAACCCGGGG TTTGTCACCT TCGGCTGGTA

951 CCGCCTCAAG CCCGGCCGCG GGAACGCGCC GGCCCAACCG CGCCCCCCGA

45   1001 CGGCGTTCGG AACCTCGAGC GACGTCGAGT TTAACTGCAC GGCGGACAAC

1051 CTGGCCGTCG AGGGGGCCAT GTGTGACCTG CCGGCCTACA AGCTCATGTG

1101 CTTCGATATC GAATGCAAGG CCGGGGGGGA GGACGAGCTG GCCTTTCCGG

50

1151 TCGCGGAACG CCCGGAAGAC CTCGTCATCC AGATCTCCTG TCTGCTCTAC

1201 GACCTGTCCA CCACCGCCCT CGAGCACATC CTCCTGTTTT CGCTCGGATC

55   1251 CTGCGACCTC CCCGAGTCCC ACCTCAGCGA TCTCGCCTCC AGGGGCCTGC

1301 CGGCCCCCGT CGTCCTGGAG TTTGACAGCG AATTCGAGAT GCTGCTGGCC

1351 TTCATGACCT TCGTCAAGCA GTACGGCCCC GAGTTCGTGA CCGGGTACAA

1401 CATCATCAAC TTCGACTGGC CCTTCGTCCT GACCAAGCTG ACGGAGATCT

5   1451 ACAAGGTCCC GCTCGACGGG TACGGGCGCA TGAACGGCCG GGGTGTGTTC

1501 CGCGTGTGGG ACATCGGCCA GAGCCACTTT CAGAAGCGCA GCAAGATCAA

1551 GGTGAACGGG ATGGTGAACA TCGACATGTA CGGCATCATC ACCGACAAGG

10 1601 TCAAACTCTC CAGCTACAAG CTGAACGCCG TCGCCGAGGC CGTCTTGAAG

1651 GACAAGAAGA AGGATCTGAG CTACCGCGAC ATCCCCGCCT ACTACGCCTC

15 1701 CGGGCCCGCG CAGCGCGGGG TGATCGGCGA GTATTGTGTG CAGGACTCGC

1751 TGCTGGTCGG GCAGCTGTTC TTCAAGTTTC TGCCGCACCT GGAGCTTTCC

1801 GCCGTCGCGC GCCTGGCGGG CATCAACATC ACCCGCACCA TCTACGACGG

20 1851 CCAGCAGATC CGCGTCTTCA CGTGCCTCCT GCGCCTTGCG GGCCAGAAGG

1901 GCTTCATCCT GCCGGACACC CAGGGGCGGT TCGGGGCCT CGACAAGGAG

25 1951 GCGCCCAAGC GCCCGGCCGT GCCTCGGGGG GAAGGGGAGC GGCCGGGGGA

2001 CGGGAACGGG GACGAGGATA AGGACGACGA CGAGGACGAG GACGGGGACG

2051 AGCGCGAGGA GGTCGCGCGC GAGACCGGGG GCCGGCACGT TGGGTACCAG

30 2101 GGGGCCCGGG TCCTCGACCC CACCTCCGGG TTTCACGTCG ACCCCGTGGT

2151 GGTGTTTGAC TTTGCCAGCC TGTACCCCAG CATCATCCAG GCCCACAACC

35 2201 TGTGCTTCAG TACGCTCTCC CTGCGGCCCG AGGCCGTCGC GCACCTGGAG

2251 GCGGACCGGG ACTACCTGGA GATCGAGGTG GGGGGCCGAC GGCTGTTCTT

2301 CGTGAAGGCC CACGTACGCG AGAGCCTGCT GAGCATCCTG CTGCGCGACT

40 2351 GGCTGGCCAT GCGAAAGCAG ATCCGCTCGC GGATCCCCCA GAGCACCCCC

2401 GAGGAGGCCG TCCTCCTCGA CAAGCAACAG GCCGCCATCA AGGTGGTGTG

45 2451 CAACTCGGTG TACGGGTTCA CCGGGGCGCA GCACGGTCTT CTGCCCTGCC

2501 TGCACGTGGC CGCCACCGTG ACGACCATCG GCCGCGAGAT GCTCCTCGCG

2551 ACGCGCGCGT ACGTGCACGC GCGCTGGGCG GAGTTCGATC AGCTGCTGGC

50 2601 CGACTTTCCG GAGGCGGCCG GCATGCGCGC CCCCGGTCCG TACTCCATGC

2651 GCATCATCTA CGGGGACACG GACTCCATTT TCGTTTTGTG CCGCGGCCTC

55 2701 ACGGCCGCGG GCCTGGTGGC CATGGGCGAC AAGATGGCGA GCCACATCTC

2751 GCGCGCGCTG TTCCTCCCCC CGATCAAGCT CGAGTGCGAA AAAACGTTCA

2801 CCAAGCTGCT GCTCATCGCC AAGAAAAAGT ACATCGGCGT CATCTGCGGG

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2851 GGCAAGATGC TCATCAAGGG CGTGGATCTG GTGCGCAAAA ACAACTGCGC

2901 GTTTATCAAC CGCACCTCCA GGGCCCTGGT CGACCTGCTG TTTTACGACG

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2951 ATACCGTATC CGGAGCGGCC GCCGCGTTAG CCGAGCGCCC CGCAGAGGAG

3001 TGGCTGGCGC GACCCCTGCC CGAGGGACTG CAGGCGTTCG GGGCCGTCCT

3051 CGTAGACGCC CATCGGCGCA TCACCGACCC GGAGAGGGAC ATCCAGGACT

10

3101 TTGTCCTCAC CGCCGAACTG AGCAGACACC CGCGCGCGTA CACCAACAAG

3151 CGCCTGGCCC ACCTGACGGT GTATTACAAG CTCATGGCCC CCGCGCGCA

15

3201 GGTCCCGTCC ATCAAGGACC GGATCCCGTA CGTGATCGTG GCCCAGACCC

3251 GCGAGGTAGA GGAGACGGTC GCGCGGCTGG CCGCCCTCCG CGAGCTAGAC

3301 GCCGCCGCCC CAGGGGACGA GCCCGCCCCC CCAGCGGCCC TGCCCTCCCC

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3351 GGCCAAGCGC CCCCGGGAGA CGCCGTCGCA TGCCGACCCC CCGGGAGGCG

3401 CGTCCAAGCC CCGCAAGCTG CTGGTGTCCG AGCTGGCGGA GGATCCCGGG

3451 TACGCCATCG CCCGGGGCGT TCCGCTCAAC ACGGACTATT ACTTCTCGCA

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3501 CCTGCTGGGG GCGGCCTGCG TGACGTTCAA GGCCCTGTTT GGAAATAACG

3551 CCAAGATCAC CGAGAGTCTG TTAAAGAGGT TTATTCCCGA GACGTGGCAC

30

3601 CCCCCGGACG ACGTGGCCGC GCGGCTCAGG GCCGCGGGGT TCGGGCCGGC

3651 GGGGGCCGGC GCTACGGCGG AGGAAACTCG TCGAATGTTG CATAGAGCCT

35   3701 TTGATACTCT AGCATGA

SEQ. ID. NO. 2   Amino acid sequence of DNA polymerase for HSV2-MS-M1

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   1 MFCAAGGPTS PGGKSAARAA SGFFAPHNPR GATQTAPPPC RRQNFYNPHL

  51 AQTGTQPKAP GPAQRHTYYS ECDEFRFIAP RSLDEDAPAE QRTGVHDGRL

 101 RRAPKVYCGG DERDVLRVGP EGFWPRRLRL WGGADHAPKG FDPTVTVFHV

 151 YDILEHVEHA YSMRAAQLHE RFMDAITPAG TVITLLGLTP EGHRVAVHVY

 201 GTRQYFYMNK AEVDRHLQCR APRDLCERLA AALRESPGAS FRGISADHFE

 251 AEVVERADVY YYETRPTLYY RVFVRSGRAL AYLCDNFCPA IRKYEGGVDA

 301 TTRFILDNPG FVTFGWYRLK PGRGNAPAQP RPPTAFGTSS DVEFNCTADN

 351 LAVEGAMCDL PAYKLMCFDI ECKAGGEDEL AFPVAERPED LVIQISCLLY

 401 DLSTTALEHI LLFSLGSCDL PESHLSDLAS RGLPAPVVLE FDSEFEMLLA

 451 FMTFVKQYGP EFVTGYNIIN FDWPFVLTKL TEIYKVPLDG YGRMNGRGVF

 501 RVWDIGQSHF QKRSKIKVNG MVNIDMYGII TDKVKLSSYK LNAVAEAVLK

 551 DKKKDLSYRD IPAYYASGPA QRGVIGEYCV QDSLLVGQLF FKFLPHLELS

 601 AVARLAGINI TRTIYDGQQI RVFTCLLRLA GQKGFILPDT QGRFRGLDKE

 651 APKRPAVPRG EGERPGDGNG DEDKDDDEDE DGDEREEVAR ETGGRHVGYQ

 701 GARVLDPTSG FHVDPVVVFD FASLYPSIIQ AHNLCFSTLS LRPEAVAHLE

 751 ADRDYLEIEV GGRRLFFVKA HVRESLLSIL LRDWLAMRKQ IRSRIPQSTP

 801 EEAVLLDKQQ AAIKVVCNSV YGFTGAQHGL LPCLHVAATV TTIGREMLLA

 851 TRAYVHARWA EFDQLLADFP EAAGMRAPGP YSMRIIYGDT DSIFVLCRGL

 901 TAAGLVAMGD KMASHISRAL FLPPIKLECE KTFTKLLLIA KKKYIGVICG

 951 GKMLIKGVDL VRKNNCAFIN RTSRALVDLL FYDDTVSGAA AALAERPAEE

1001 WLARPLPEGL QAFGAVLVDA HRRITDPERD IQDFVLTAEL SRHPRAYTNK

1051 RLAHLTVYYK LMARRAQVPS IKDRIPYVIV AQTREVEETV ARLAALRELD

1101 AAAPGDEPAP PAALPSPAKR PRETPSHADP PGGASKPRKL LVSELAEDPG

1151 YAIARGVPLN TDYYFSHLLG AACVTFKALF GNNAKITESL LKRFIPETWH

1201 PPDDVAARLR AAGFGPAGAG ATAEETRRML HRAFDTLA*
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SEQ.ID.NO. 3   DNA sequence of DNA polymerase gene for HSV2-186-M1

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   1 ATGTTTTGTG CCGCGGGCGG CCCGGCTTCC CCCGGGGGGA AGTCGGCGGC

  51 TCGGGCGGCG TCTGGGTTTT TTGCCCCCCA CAACCCCCGG GGAGCCACCC

 101 AGACGGCACC GCCGCCTTGC CGCCGGCAGA ACTTCTACAA CCCCCACCTC

 151 GCTCAGACCG GAACGCAGCC AAAGGCCCCC GGGCCGGCTC AGCGCCATAC

 201 GTACTACAGC GAGTGCGACG AATTTCGATT TATCGCCCCG CGTTCGCTGG

 251 ACGAGGACGC CCCCGCGGAG CAGCGCACCG GGGTCCACGA CGGCCGCCTC

 301 CGGCGCGCCC CTAAGGTGTA CTGCGGGGGG GACGAGCGCG ACGTCCTCCG

 351 CGTGGGCCCG GAGGGCTTCT GGCCGCGTCG CTTGCGCCTG TGGGGCGGTG

 401 CGGACCATGC CCCCGAGGGG TTCGACCCCA CCGTCACCGT CTTCCACGTG

 451 TACGACATCC TGGAGCACGT GGAACACGCG TACAGCATGC GCGCCGCCCA

 501 GCTCCACGAG CGATTTATGG ACGCCATCAC GCCCGCCGGG ACCGTCATCA

 551 CGCTTCTGGG TCTGACCCCC GAAGGCCATC GCGTCGCCGT TCACGTCTAC

 601 GGCACGCGGC AGTACTTTTA CATGAACAAG GCGGAGGTGG ATCGGCACCT

 651 GCAGTGCCGT GCCCCGCGCG ATCTCTGCGA GCGCCTGGCG GCGGCCCTGC

 701 GCGAGTCGCC GGGGGCGTCG TTCCGCGGCA TCTCCGCGGA CCACTTCGAG

 751 GCGGAGGTGG TGGAGCGCGC CGACGTGTAC TATTACGAAA CGCGCCCGAC

 801 CCTGTACTAC CGCGTCTTCG TGCGAAGCGG CGCGCGCTG GCCTACCTGT

 851 GCGACAACTT TTGCCCCGCG ATCAGGAAGT ACGAGGGGGG CGTCGACGCC

 901 ACCACCCGGT TTATCCTGGA CAACCCGGGG TTTGTCACCT TCGGCTGGTA

 951 CCGCCTCAAG CCCGGCCGCG GGAACGCGCC GGCCCAACCG CGCCCCCCGA

1001 CGGCGTTCGG AACCTCGAGC GACGTCGAGT TTAACTGCAC GGCGGACAAC

1051 CTGGCCGTCG AGGGGGCCAT GTGTGACCTG CCGGCCTACA AGCTCATGTG

1101 CTTCGATATC GAATGCAAGG CCGGGGGGGA GGACGAGCTG GCCTTTCCGG

1151 TCGCGGAACG CCCGGAAGAC CTCGTCATCC AGATCTCCTG TCTGCTCTAC

1201 GACCTGTCCA CCACCGCCCT CGAGCACATC CTCCTGTTTT CGCTCGGATC

1251 CTGCGACCTC CCCGAGTCCC ACCTCAGCGA TCTCGCCTCC AGGGGCCTGC

1301 CGGCCCCCGT CGTCCTGGAG TTTGACAGCG AATTCGAGAT GCTGCTGGCC

1351 TTCATGACCT TCGTCAAGCA GTACGGCCCC GAGTTCGTGA CCGGGTACAA

1401 CATCATCAAC TTCGACTGGC CCTTCGTCCT GACCAAGCTG ACGGAGATCT
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1451 ACAAGGTCCC GCTCGACGGG TACGGGCGCA TGAACGGCCG GGGTGTGTTC

1501 CGCGTGTGGG ACATCGGCCA GAGCCACTTT CAGAAGCGCA GCAAGATCAA

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1551 GGTGAACGGG ATGGTGAACA TCGACATGTA CGGCATCATC ACCGACAAGG

1601 TCAAACTCTC CAGCTACAAG CTGAACGCCG TCGCCGAGGC CGTCTTGAAG

1651 GACAAGAAGA AGGATCTGAG CTACCGCGAC ATCCCCGCCT ACTACGCCTC

10

1701 CGGGCCCGCG CAGCGCGGGG TGATCGGCGA GTATTGTGTG CAGGACTCGC

1751 TGCTGGTCGG GCAGCTGTTC TTCAAGTTTC TGCCGCACCT GGAGCTTTCC

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1801 GCCGTCGCGC GCCTGGCGGG CATCAACATC ACCCGCACCA TCTACGACGG

1851 CCAGCAGATC CGCGTCTTCA CGTGCCTCCT GCGCCTTGCG GGCCAGAAGG

1901 GCTTCATCCT GCCGGACACC CAGGGGCGGT TTCGGGGCCT CGACAAGGAG

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1951 GCGCCCAAGC GCCCGGCCGT GCCTCGGGGG GAAGGGGAGC GGCCGGGGGA

2001 CGGGAACGGG GACGAGGATA AGGACGACGA CGAGGACGGG GACGAGGACG

2051 GGGACGAGCG CGAGGAGGTC GCGCGCGAGA CCGGGGGCCG GCACGTTGGG

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2101 TACCAGGGGG CCCGGGTCCT CGACCCCACC TCCGGGTTTC ACGTCGACCC

2151 CGTGGTGGTG TTTGACTTTG CCAGCCTGTA CCCCAGCATC ATCCAGGCCC

30

2201 ACAACCTGTG CTTCAGTACG CTCTCCCTGC GGCCCGAGGC CGTCGCGCAC

2251 CTGGAGGCGG ACCGGGACTA CCTGGAGATC GAGGTGGGGG GCCGACGGCT

2301 GTTCTTCGTG AAGGCCCACG TACGCGAGAG CCTGCTGAGC ATCCTGCTGC

35

2351 GCGACTGGCT GGCCATGCGA AAGCAGATCC GCTCGCGGAT CCCCCAGAGC

2401 CCCCCCGAGG AGGCCGTCCT CCTCGACAAG CAACAGGCCG CCATCAAGGT

40

2451 GGTGTGCAAC TCGGTGTACG GGTTCACCGG GGCGCAGCAC GGTCTTCTGC

2501 CCTGCCTGCA CGTGGCCGCC ACCGTGACGA CCATCGGCCG CGAGATGCTC

2551 CTCGCGACGC GCGCGTACGT GCACGCGCGC TGGGCGGAGT TCGATCAGCT

45

2601 GCTGGCCGAC TTTCCGGAGG CGGCCGGCAT GCGCGCCCCC GGTCCGTACT

2651 CCATGCGCAT CATCTACGGG GACACGGACT CCATTTTCGT TTTGTGCCGC

2701 GGCCTCACGG CCGCGGGCCT GGTGGCCATG GGCGACAAGA TGGCGAGCCA

50

2751 CATCTCGCGC GCGCTGTTCC TCCCCCCGAT CAAGCTCGAG TGCGAAAAAA

2801 CGTTCACCAA GCTGCTGCTC ATCGCCAAGA AAAAGTACAT CGGCGTCATC

55

2851 TGCGGGGGCA AGATGCTCAT CAAGGGCGTG GATCTGGTGC GCAAAAACAA

2901 CTGCGCGTTT ATCAACCGCA CCTCCAGGGC CCTGGTCGAC CTGCTGTTTT

60

2951 ACGACGATAC CGTATCCGGA GCGGCCGCCG CGTTAGCCGA GCGCCCCGCA

3001 GAGGAGTGGC TGGCGCGACC CCTGCCCGAG GGACTGCAGG CGTTCGGGGC

5   3051 CGTCCTCGTA GACGCCCATC GGCGCATCAC CGACCCGGAG AGGGACATCC

3101 AGGACTTTGT CCTCACCGCC GAACTGAGCA GACACCCGCG CGCGTACACC

3151 AACAAGCGCC TGGCCCACCT GACGGTGTAT TACAAGCTCA TGGCCCGCCG

10 3201 CGCGCAGGTC CCGTCCATCA AGGACCGGAT CCCGTACGTG ATCGTGGCCC

3251 AGACCCGCGA GGTAGAGGAG ACGGTCGCGC GGCTGGCCGC CCTCCGCGAG

15 3301 CTAGACGCCG CCGCCCCAGG GGACGAGCCC GCCCCCCCAG CGGCCCTGCC

3351 CTCCCCGGCC AAGCGCCCCC GGGAGACGCC GTCGCATGCC GACCCCCCGG

3401 GAGGCGCGTC CAAGCCCCGC AAGCTGCTGG TGTCCGAGCT GGCGGAGGAT

20 3451 CCCGGGTACG CCATCGCCCG GGGCGTTCCG CTCAACACGG ACTATTACTT

3501 CTCGCACCTG CTGGGGGCGG CCTGCGTGAC GTTCAAGGCC CTGTTTGGAA

25 3551 ATAACGCCAA GATCACCGAG AGTCTGTTAA AGAGGTTTAT TCCCGAGACG

3601 TGGCACCCCC CGGACGACGT GGCCGCGCGG CTCAGGGCCG CGGGGTTCGG

3651 GCCGGCGGGG GCCGGCGCTA CGGCGGAGGA AACTCGTCGA ATGTTGCATA

30 3701 GAGCCTTTGA TACTCTAGCA TGA

SEQ.ID.NO. 4   Amino acid sequence of DNA polymerase for HSV2-186-M1

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  1 MFCAAGGPAS PGGKSAARAA SGFFAPHNPR GATQTAPPPC RRQNFYNPHL

 51 AQTGTQPKAP GPAQRHTYYS ECDEFRFIAP RSLDEDAPAE QRTGVHDGRL

101 RRAPKVYCGG DERDVLRVGP EGFWPRRLRL WGGADHAPEG FDPTVTVFHV

151 YDILEHVEHA YSMRAAQLHE RFMDAITPAG TVITLLGLTP EGHRVAVHVY

201 GTRQYFYMNK AEVDRHLQCR APRDLCERLA AALRESPGAS FRGISADHFE

251 AEVVERADVY YYETRPTLYY RVFVRSGRAL AYLCDNFCPA IRKYEGGVDA

301 TTRFILDNPG FVTFGWYRLK PGRGNAPAQP RPPTAFGTSS DVEFNCTADN

351 LAVEGAMCDL PAYKLMCFDI ECKAGGEDEL AFPVAERPED LVIQISCLLY

401 DLSTTALEHI LLFSLGSCDL PESHLSDLAS RGLPAPVVLE FDSEFEMLLA

451 FMTFVKQYGP EFVTGYNIIN FDWPFVLTKL TEIYKVPLDG YGRMNGRGVF

501 RVWDIGQSHF QKRSKIKVNG MVNIDMYGII TDKVKLSSYK LNAVAEAVLK

551 DKKKDLSYRD IPAYYASGPA QRGVIGEYCV QDSLLVGQLF FKFLPHLELS

601 AVARLAGINI TRTTYDGQQI RVFTCLLRLA GQKGFILPDT QGRFRGLDKE

651 APKRPAVPRG EGERPGDGNG DEDKDDDEDG DEDGDEREEV ARETGGRHVG

701 YQGARVLDPT SGFHVDPVVV FDFASLYPSI IQAHNLCFST LSLRPEAVAH

751 LEADRDYLEI EVGGRRLFFV KAHVRESLLS ILLRDWLAMR KQIRSRIPQS

801 PPEEAVLLDK QQAAIKVVCN SVYGFTGAQH GLLPCLHVAA TVTTIGREML

851 LATRAYVHAR WAEFDQLLAD FPEAAGMRAP GPYSMRIIYG DTDSIFVLCR

901 GLTAAGLVAM GDKMASHISR ALFLPPIKLE CEKTFTKLLL IAKKKYIGVI

951 CGGKMLIKGV DLVRKNNCAF INRTSRALVD LLFYDDTVSG AAAALAERPA

1001 EEWLARPLPE GLQAFGAVLV DAHRRITDPE RDIQDFVLTA ELSRHPRAYT

1051 NKRLAHLTVY YKLMARRAQV PSIKDRIPYV IVAQTREVEE TVARLAALRE

1101 LDAAAPGDEP APPAALPSPA KRPRETPSHA DPPGGASKPR KLLVSELAED

1151 PGYAIARGVP LNTDYYFSHL LGAACVTFKA LFGNNAKITE SLLKRFIPET

1201 WHPPDDVAAR LRAAGFGPAG AGATAEETRR MLHRAFDTLA *
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SEQ.ID.NO. 5   DNA sequence of DNA polymerase gene for HSV1-KOS-M1

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  1 ATGTTTTCCG GTGGCGGCGG CCCGCTGTCC CCCGGAGGAA AGTCGGCGGC

 51 CAGGGCGGCG TCCGGGTTTT TTGCGCCCGC CGGCCCTCGC GGAGCCGGCC

101 GGGGACCCCC GCCTTGTTTG AGGCAAAACT TTTACAACCC CTACCTCGCC

151 CCAGTCGGGA CGCAACAGAA GCCGACCGGG CCAACCCAGC GCCATACGTA

201 CTATAGCGAA TGCGATGAAT TTCGATTCAT CGCCCCGCGG GTGCTGGACG

251 AGGATGCCCC CCCGGAGAAG CGCGCCGGGG TGCACGACGG TCACCTCAAG

301 CGCGCCCCCA AGGTGTACTG CGGGGGGGAC GAGCGCGACG TCCTCCGCGT

351 CGGGTCGGGC GGCTTCTGGC CGCGGCGCTC GCGCCTGTGG GGCGGCGTGG

401 ACCACGCCCC GGCGGGGTTC AACCCCACCG TCACCGTCTT TCACGTGTAC

451 GACATCCTGG AGAACGTGGA GCACGCGTAC GGCATGCGCG CGGCCCAGTT

501 CCACGCGCGG TTTATGGACG CCATCACACC GACGGGGACC GTCATCACGC

551 TCCTGGGCCT GACTCCGGAA GGCCACCGGG TGGCCGTTCA CGTTTACGGC

601 ACGCGGCAGT ACTTTTACAT GAACAAGGAG GAGGTTGACA GGCACCTACA

651 ATGCCGCGCC CCACGAGATC TCTGCGAGCG CATGGCCGCG GCCCTGCGCG

701 AGTCCCCGGG CGCGTCGTTC CGCGGCATCT CCGCGGACCA CTTCGAGGCG

751 GAGGTGGTGG AGCGCACCGA CGTGTACTAC TACGAGACGC GCCCCGCTCT

801 GTTTTACCGC GTCTACGTCC GAAGCGGGCG CGTGCTGTCG TACCTGTGCG

851 ACAACTTCTG CCCGGCCATC AAGAAGTACG AGGGTGGGGT CGACGCCACC

901 ACCCGGTTCA TCCTGGACAA CCCCGGGTTC GTCACCTTCG CTGGTACCG

951 TCTCAAACCG GGCCGGAACA ACACGCTAGC CCAGCCGCGG GCCCCGATGG

1001 CCTTCGGGAC ATCCAGCGAC GTCGAGTTTA ACTGTACGGC GGACAACCTG

1051 GCCATCGAGG GGGGCATGAG CGACCTACCG GCATACAAGC TCATGTGCTT

1101 CGATATCGAA TGCAAGGCGG GGGGGGAGGA CGAGCTGGCC TTTCCGGTGG

1151 CCGGGCACCC GGAGGACCTG GTTATTCAGA TATCCTGTCT GCTCTACGAC

1201 CTGTCCACCA CCGCCCTGGA GCACGTCCTC CTGTTTTCGC TCGGTTCCTG

1251 CGACCTCCCC GAATCCCACC TGAACGAGCT GGCGGCCAGG GGCCTGCCCA

1301 CGCCCGTGGT TCTGGAATTC GACAGCGAAT TCGAGATGCT GTTGGCCTTC

1351 ATGACCCTTG TGAAACAGTA CGGCCCCGAG TTCGTGACCG GGTACAACAT

1401 CATCAACTTC GACTGGCCCT TCTTGCTGGC CAAGTTGACG GACATTTACA
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1451 AGGTCCCCCT GGACGGGTAC GGCCGCATGA ACGGCCGGGG CGTGTTTCGC

1501 GTGTGGGACA TAGGCCAGAG CCACTTCCAG AAGCGCAGCA AGATAAAGGT

1551 GAACGGCATG GTGAACATCG ACATGTACGG GATCATAACC GACAAGATCA

1601 AGCTCTCGAG CTACAAGCTC AACGCCGTGG CCGAAGCCGT CCTGAAGGAC

1651 AAGAAGAAGG ACCTGAGCTA TCGCGACATC CCCGCCTACT ACGCCGCCGG

1701 GCCCGCGCAA CGCGGGGTGA TCGGCGAGTA CTGCATACAG GATTCCCTGC

1751 TGGTGGGCCA GCTGTTTTTT AAGTTTTTGC CCCATCTGGA GCTCTCGGCC

1801 GTCGCGCGCT TGGCGGGTAT TAACATCACC CGCACCATCT ACGACGGCCA

1851 GCAGATCCGC GTCTTTACGT GCCTGCTGCG CCTGGCCGAC CAGAAGGGCT

1901 TTATTCTGCC GGACACCCAG GGGCGATTTA GGGGCGCCGG GGGGGAGGCG

1951 CCCAAGCGTC CGGCCGCAGC CCGGGAGGAC GAGGAGCGGC CAGAGGAGGA

2001 GGGGGAGGAC GAGGACGAAC GCGAGGAGGG CGGGGGCGAG CGGGAGCCGG

2051 AGGGCGCGCG GGAGACCGCC GGCCGGCACG TGGGGTACCA GGGGGCCAGG

2101 GTCCTTGACC CCACTTCCGG GTTTCACGTG AACCCCGTGG TGGTGTTCGA

2151 CTTTGCCAGC CTGTACCCCA GCATCATCCA GGCCCACAAC CTGTGCTTCA

2201 GCACGCTCTC CCTGAGGGCC GACGCAGTGG CGCACCTGGA GGCGGGCAAG

2251 GACTACCTGG AGATCGAGGT GGGGGGGCGA CGGCTGTTCT TCGTCAAGGC

2301 TCACGTGCGA GAGAGCCTCC TCAGCATCCT CCTGCGGGAC TGGCTCGCCA

2351 TGCGAAAGCA GATCCGCTCG CGGATTCCCC AGAGCAGCCC CGAGGAGGCC

2401 GTGCTCCTGG ACAAGCAGCA GGCCGCCATC AAGGTCGTGT GTAACTCGGT

2451 GTACGGGTTC ACGGGAGCGC AGCACGGACT CCTGCCGTGC CTGCACGTTG

2501 CCGCGACGGT GACGACCATC GGCCGCGAGA TGCTGCTCGC GACCCGCGAG

2551 TACGTCCACG CGCGCTGGGC GGCCTTCGAA CAGCTCCTGG CCGATTTCCC

2601 GGAGGCGGCC GACATGCGCG CCCCCGGGCC CTATTCCATG CGCATCATCT

2651 ACGGGGACAC GGACTCCATA TTTGTGCTGT GCCGCGGCCT CACGGCCGCC

2701 GGGCTGACGG CCATGGGCGA CAAGATGGCG AGCCACATCT CGCGCGCGCT

2751 GTTTCTGCCC CCCATCAAAC TCGAGTGCGA AAAGACGTTC ACCAAGCTGC

2801 TGCTGATCGC CAAGAAAAAG TACATCGGCG TCATCTACGG GGGTAAGATG

2851 CTCATCAAGG GCGTGGATCT GGTGCGCAAA AACAACTGCG CGTTTATCAA

2901 CCGCACCTCC AGGGCCCTGG TCGACCTGCT GTTTTACGAC GATACCGTAT

2951 CCGGAGCGGC CGCCGCGTTA GCCGAGCGCC CCGCAGAGGA GTGGCTGGCG

3001 CGACCCCTGC CCGAGGGACT GCAGGCGTTC GGGGCCGTCC TCGTAGACGC

5   3051 CCATCGGCGC ATCACCGACC CGGAGAGGGA CATCCAGGAC TTTGTCCTCA

3101 CCGCCGAACT GAGCAGACAC CCGCGCGCGT ACACCAACAA GCGCCTGGCC

3151 CACCTGACGG TGTATTACAA GCTCATGGCC CGCCGCGCGC AGGTCCCGTC

10   3201 CATCAAGGAC CGGATCCCGT ACGTGATCGT GGCCCAGACC CGCGAGGTAG

3251 AGGAGACGGT CGCGCGGCTG GCCGCCCTCC GCGAGCTAGA CGCCGCCGCC

15   3301 CCAGGGGACG AGCCCGCCCC CCCCGCGGCC CTGCCCTCCC CGGCCAAGCG

3351 CCCCCGGGAG ACGCCGTCGC ATGCCGACCC CCCGGGAGGC GCGTCCAAGC

3401 CCCGCAAGCT GCTGGTGTCC GAGCTGGCCG AGGATCCCGC ATACGCCATT

20   3451 GCCCACGGCG TCGCCCTGAA CACGGACTAT TACTTCTCCC ACCTGTTGGG

3501 GGCGGCGTGC GTGACATTCA AGGCCCTGTT TGGGAATAAC GCCAAGATCA

25   3551 CCGAGAGTCT GTTAAAAAGG TTTATTCCCG AAGTGTGGCA CCCCCCGGAC

3601 GACGTGGCCG CGCGGCTCCG GGCCGCAGGG TTCGGGGCGG TGGGTGCCGG

3651 CGCTACGGCG GAGGAAACTC GTCGAATGTT GCATAGAGCC TTTGATACTC

30   3701 TAGCATGA

SEQ.ID.NO. 6   Amino acid sequence of DNA polymerase for HSV1-KOS-M1

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   1 MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGRGPPPCL RQNFYNPYLA
  51 PVGTQQKPTG PTQRHTYYSE CDEFRFIAPR VLDEDAPPEK RAGVHDGHLK
 101 RAPKVYCGGD ERDVLRVGSG GFWPRRSRLW GGVDHAPAGF NPTVTVFHVY
 151 DILENVEHAY GMRAAQFHAR FMDAITPTGT VITLLGLTPE GHRVAVHVYG
 201 TRQYFYMNKE EVDRHLQCRA PRDLCERMAA ALRESPGASF RGISADHFEA
 251 EVVERTDVYY YETRPALFYR VYVRSGRVLS YLCDNFCPAI KKYEGGVDAT
 301 TRFILDNPGF VTFGWYRLKP GRNNTLAQPR APMAFGTSSD VEFNCTADNL .
 351 AIEGGMSDLP AYKLMCFDIE CKAGGEDELA FPVAGHPEDL VIQISCLLYD
 401 LSTTALEHVL LFSLGSCDLP ESHLNELAAR GLPTPVVLEF DSEFEMLLAF
 451 MTLVKQYGPE FVTGYNIINF DWPFLLAKLT DIYKVPLDGY GRMNGRGVFR
 501 VWDIGQSHFQ KRSKIKVNGM VNIDMYGIIT DKIKLSSYKL NAVAEAVLKD
 551 KKKDLSYRDI PAYYAAGPAQ RGVIGEYCIQ DSLLVGQLFF KFLPHLELSA
 601 VARLAGINIT RTIYDGQQIR VFTCLLRLAD QKGFILPDTQ GRFRGAGGEA
 651 PKRPAAARED EERPEEEGED EDEREEGGGE REPEGARETA GRHVGYQGAR
 701 VLDPTSGFHV NPVVVFDFAS LYPSIIQAHN LCFSTLSLRA DAVAHLEAGK
 751 DYLEIEVGGR RLFFVKAHVR ESLLSILLRD WLAMRKQIRS RIPQSSPEEA
 801 VLLDKQQAAI KVVCNSVYGF TGAQHGLLPC LHVAATVTTI GREMLLATRE
 851 YVHARWAAFE QLLADFPEAA DMRAPGPYSM RIIYGDTDSI FVLCRGLTAA
 901 GLTAMGDKMA SHISRALFLP PIKLECEKTF TKLLLIAKKK YIGVIYGGKM
 951 LIKGVDLVRK NNCAFINRTS RALVDLLFYD DTVSGAAAAL AERPAEEWLA
1001 RPLPEGLQAF GAVLVDAHRR ITDPERDIQD FVLTAELSRH PRAYTNKRLA
1051 HLTVYYKLMA RRAQVPSIKD RIPYVIVAQT REVEETVARL AALRELDAAA
1101 PGDEPAPPAA LPSPAKRPRE TPSHADPPGG ASKPRKLLVS ELAEDPAYAI
1151 AHGVALNTDY YFSHLLGAAC VTFKALFGNN AKITESLLKR FIPEVWHPPD
1201 DVAARLRAAG FGAVGAGATA EETRRMLHRA FDTLA*
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SEQ.ID.NO. 7   DNA sequence of HSV polymerase gene for HSV1-F-M1

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   1  ATGTTTTCCG GTGGCGGCGG CCCGCTGTCC CCCGGAGGAA AGTCGGCGGC

  51  CAGGGCGGCG TCCGGGTTTT TTGCGCCCGC CGGCCCTCGC GGAGCCGGCC

 101  GGGGACCCCC GCCTTGCTTG AGGCAAAACT TTTACAACCC CTACCTCGCC

 151  CCAGTCGGGA CGCAACAGAA GCCGACCGGG CCAACCCAGC GCCATACGTA

 201  CTATAGCGAA TGCGATGAAT TTCGATTCAT CGCCCCGCGG GTGCTGGACG

 251  AGGATGCCCC CCCGGAGAAG CGCGCCGGGG TGCACGACGG TCACCTCAAG

 301  CGCGCCCCCA AGGTGTACTG CGGGGGGGAC GAGCGCGACG TCCTCCGCGT

 351  CGGGTCGGGC GGCTTCTGGC CGCGGCGCTC GCGCCTGTGG GGCGGCGTGG

 401  ACCACGCCCC GGCGGGGTTC AACCCCACCG TCACCGTCTT TCACGTGTAC

 451  GACATCCTGG AGAACGTGGA GCACGCGTAC GGCATGCGCG CGGCCCAGTT

 501  CCACGCGCGG TTTATGGACG CCATCACACC GACGGGGACC GTCATCACGC

 551  TCCTGGGCCT GACTCCGGAA GGCCACCGGG TGGCCGTTCA CGTTTACGGC

 601  ACGCGGCAGT ACTTTTACAT GAACAAGGAG GAGGTCGACA GGCACCTACA

 651  ATGCCGCGCC CCACGAGATC TCTGCGAGCG CATGGCCGCG GCCCTGCGCG

 701  AGTCCCCGGG CGCGTCGTTC CGCGGCATTT CCGCGGACCA CTTCGAGGCG

 751  GAGGTGGTGG AGCGCACCGA CGTGTACTAC TACGAGACGC GCCCCGCTCT

 801  GTTTTACCGC GTCTACGTCC GAAGCGGGCG CGTGCTGTCG TACCTGTGCG

 851  ACAACTTCTG CCCGGCCATC AAGAAGTACG AGGGTGGGGT CGACGCCACC

 901  ACCCGGTTCA TCCTGGACAA CCCCGGGTTC GTCACCTTCG GCTGGTACCG

 951  TCTCAAACCG GGCCGGAACA ACACGCTAGC CCAGCCGCGG GCCCCGATGG

1001  CCTTCGGGAC ATCCAGCGAC GTCGAGTTTA ACTGTACGGC GGACAACCTG

1051  GCCATCGAGG GGGGCATGAG CGACCTACCG GCATACAAGC TCATGTGCTT

1101  CGATATCGAA TGCAAGGCGG GGGGGGAGGA CGAGCTGGCC TTTCCGGTGG

1151  CCGGGCACCC GGAGGACCTG GTCATCCAGA TATCCTGTCT GCTCTACGAC

1201  CTGTCCACCA CCGCCCTGGA GCACGTCCTC CTGTTTTCGC TCGGTTCCTG

1251  CGACCTCCCC GAATCCCACC TGAACGAGCT GGCGGCCAGG GGCCTGCCCA

1301  CGCCCGTGGT TCTGGAATTC GACAGCGAAT CGAGATGCT GTTGGCCTTC

1351  ATGACCCTTG TGAAACAGTA CGGCCCCGAG TTCGTGACCG GGTACAACAT

1401  CATCAACTTC GACTGGCCCT TCTTGCTGGC CAAGCTGACG GACATTTACA

1451  AGGTCCCCCT GGACGGGTAC GGCCGCATGA ACGGCCGGGG CGTGTTTCGC

1501  GTGTGGGACA TAGGCCAGAG CCACTTCCAG AAGCGCAGCA AGATAAAGGT

1551  GAACGGCATG GTGAACATCG ACATGTACGG GATTATAACC GACAAGATCA
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1601   AGCTCTCGAG CTACAAGCTC AACGCCGTGG CCGAAGCCGT CCTGAAGGAC

1651   AAGAAGAAGG ACCTGAGCTA TCGCGACATC CCCGCCTACT ACGCCGCCGG

1701   GCCCGCGCAA CGCGGGGTGA TCGGCGAGTA CTGCATACAG GATTCCCTGC

1751   TGGTGGGCCA GCTGTTTTTT AAGTTTTTGC CCCATCTGGA GCTCTCGGCC

1801   GTCGCGCGCT TGGCGGGTAT TAACATCACC CGCACCATCT ACGACGGCCA

1851   GCAGATCCGC GTCTTTACGT GCCTGCTGCG CCTGGCCGAC CAGAAGGGCT

1901   TTATTCTGCC GGACACCCAG GGGCGATTTA GGGGCGGCGG GGGGGAGGCG

1951   CCCAAGCGTC CGGCCGCAGC CCGGGAGGAC GAGGAGCGGC CAGAGGAGGA

2001   GGGGGAGGAC GAGGACGAAC GCGAGGAGGG CGGGGGCGAG CGGGAGCCGG

2051   AGGGCGCGCG GGAGACCGCC GGCCGGCACG TGGGGTACCA GGGGGCCAGG

2101   GTCCTTGACC CCACTTCCGG GTTTCATGTG AACCCCGTGG TGGTGTTCGA

2151   CTTTGCCAGC CTGTACCCCA GCATCATCCA GGCCCACAAC CTGTGCTTCA

2201   GCACGCTCTC CCTGAGGGCC GACGCAGTGG CGCACCTGGA GGCGGGCAAG

2251   GACTACCTGG AGATCGAGGT GGGGGGGCGA CGGCTGTTCT TCGTCAAGGC

2301   TCACGTGCGA GAGAGCCTCC TCAGCATCCT CCTGCGGGAC TGGCTCGCCA

2351   TGCGAAAGCA GATCCGCTCG CGGATTCCCC AGAGCAGCCC CGAGGAGGCC

2401   GTGCTCCTGG ACAAGCAGCA GGCCGCCATC AAGGTCGTGT GTAACTCGGT

2451   TTACGGGTTC ACGGGAGCGC AGCACGGACT CCTGCCGTGC CTGCACGTTG

2501   CCGCGACGGT GACGACCATC GGCCGCGAGA TGCTGCTCGC GACCCGCGAG

2551   TACGTCCACG CGCGCTGGGC GGCCTTCGAA CAGCTCCTGG CCGATTTCCC

2601   GGAGGCGGCC GACATGCGCG CCCCCGGGCC CTATTCCATG CGCATCATCT

2651   ACGGGGACAC GGACTCCATC TTTGTGCTGT GCCGCGGCCT CACGGCCGCC

2701   GGGCTGACGG CCGTGGGCGA CAAGATGGCG AGCCACATCT CGCGCGCGCT

2751   GTTTCTGTCC CCCATCAAAC TCGAGTGCGA AAAGACGTTC ACCAAGCTGC

2801   TGCTGATCGC CAAGAAAAAG TACATCGGCG TCATCTACGG GGGTAAGATG

2851   CTCATCAAGG GCGTGGATCT GGTGCGCAAA AACAACTGCG CGTTTATCAA

2901   CCGCACCTCC AGGGCCCTGG TCGACCTGCT GTTTTACGAC GATACCGTAT

2951   CCGGAGCGGC CGCCGCGTTA GCCGAGCGCC CCGCAGAGGA GTGGCTGGCG

3001   CGACCCCTGC CCGAGGGACT GCAGGCGTTC GGGGCCGTCC TCGTAGACGC

3051   CCATCGGCGC ATCACCGACC CGGAGAGGGA CATCCAGGAC TTTGTCCTCA

3101   CCGCCGAACT GAGCAGACAC CCGCGCGCGT ACACCAACAA GCGCCTGGCC

3151   CACCTGACGG TGTATTACAA GCTCATGGCC CGCCGCGCGC AGGTCCCGTC

3201   CATCAAGGAC CGGATCCCGT ACGTGATCGT GGCCCAGACC CGCGAGGTAG
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3251   AGGAGACGGT CGCGCGGCTG GCCGCCCTCC GCGAGCTCGA CGCCGCCGCC

3301   CCAGGGGACG AGCCCGCCCC CCCCGCGGCC CTGCCCTCCC CGGCCAAGCG

3351   CCCCCGGGAG ACGCCGTTGC ATGCCGACCC CCCGGGAGGC GCGTCCAAGC

3401   CCCGCAAGCT GCTGGTGTCC GAGCTGGCCG AGGATCCCGC ATACGCCATT

3451   GCCCACGGCG TCGCCCTGAA CACGGACTAT TACTTCTCCC ACCTGTTGGG

3501   GGCGGCGTGC GTGACATTCA AGGCCCTGTT TGGGAATAAC GCCAAGATCA

3551   CCGAGAGTCT GTTAAAAAGG TTTATTCCCG AAGTGTGGCA CCCCCCGGAC

3601   GACGTGGCCG CGCGGCTCCG GGCCGCAGGG TTCGGGGCGG TGGGTGCCGG

3651   CGCTACGGCG GAGGAAACTC GTCGAATGTT GCATAGAGCC TTTGATACTC

3701   TAGCATGA
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SEQ.ID.NO. 8   Amino acid sequence of DNA polymerase for HSV1-F-M1

      1 MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGRGPPPCL RQNFYNPYLA

     51 PVGTQQKPTG PTQRHTYYSE CDEFRFIAPR VLDEDAPPEK RAGVHDGHLK

    101 RAPKVYCGGD ERDVLRVGSG GFWPRRSRLW GGVDHAPAGF NPTVTVFHVY

    151 DILENVEHAY GMRAAQFHAR FMDAITPTGT VITLLGLTPE GHRVAVHVYG

    201 TRQYFYMNKE EVDRHLQCRA PRDLCERMAA ALRESPGASF RGISADHFEA

    251 EVVERTDVYY YETRPALFYR VYVRSGRVLS YLCDNFCPAI KKYEGGVDAT

    301 TRFILDNPGF VTFGWYRLKP GRNNTLAQPR APMAFGTSSD VEFNCTADNL

    351 AIEGGMSDLP AYKLMCFDIE CKAGGEDELA FPVAGHPEDL VIQISCLLYD

    401 LSTTALEHVL LFSLGSCDLP ESHLNELAAR GLPTPVVLEF DSEFEMLLAF

    451 MTLVKQYGPE FVTGYNIINF DWPFLLAKLT DIYKVPLDGY GRMNGRGVFR

    501 VWDIGQSHFQ KRSKIKVNGM VNIDMYGIIT DKIKLSSYKL NAVAEAVLKD

    551 KKKDLSYRDI PAYYAAGPAQ RGVIGEYCIQ DSLLVGQLFF KFLPHLELSA

    601 VARLAGINIT RTTYDGQQIR VFTCLLRLAD QKGFILPDTQ GRFRGGGGEA

    651 PKRPAAARED EERPEEEGED EDEREEGGGE REPEGARETA GRHVGYQGAR

    701 VLDPTSGFHV NPVVVFDFAS LYPSIIQAHN LCFSTLSLRA DAVAHLEAGK

    751 DYLEIEVGGR RLFFVKAHVR ESLLSILLRD WLAMRKQIRS RIPQSSPEEA

    801 VLLDKQQAAI KVVCNSVYGF TGAQHGLLPC LHVAATVTTI GREMLLATRE

    851 YVHARWAAFE QLLADFPEAA DMRAPGPYSM RIIYGDTDSI FVLCRGLTAA

    901 GLTAVGDKMA SHISRALFLS PIKLECEKTF TKLLLIAKKK YIGVIYGGKM

    951 LIKGVDLVRK NNCAFINRTS RALVDLLFYD DTVSGAAAAL AERPAEEWLA

   1001 RPLPEGLQAF GAVLVDAHRR ITDPERDIQD FVLTAELSRH PRAYTNKRLA

   1051 HLTVYYKLMA RRAQVPSIKD RIPYVIVAQT REVEETVARL AALRELDAAA

   1101 PGDEPAPPAA LPSPAKRPRE TPLHADPPGG ASKPRKLLVS ELAEDPAYAI

   1151 AHGVALNTDY YFSHLLGAAC VTFKALFGNN AKITESLLKR FIPEVWHPPD

   1201 DVAARLRAAG FGAVGAGATA EETRRMLHRA FDTLA*

SEQ.ID.NO. 9   DNA sequence of HSV polymerase gene for HSV1-DJL-M1

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   1 ATGTTTTCCG GTGGCGGCGG CCCGCTGTCC CCCGGAGGAA AGTCGGCGGC
  51 CAGGGCGGCG TCCGGGTTTT TTGCGCCCGC CGGCCCTCGC GGAGCCGGCC
 101 GGGGACCCCC GCCTTGTTTG AGGCAAAACT TTTACAACCC CTACCTCGCC
 151 CCAGTCGGGA CGCAACAGAA GCCGACCGGG CCAACCCAGC GCCATACGTA
 201 CTATAGCGAA TGCGATGAAT TTCGATTCAT CGCCCCGCGG GTGCTGGACG
 251 AGGATGCCCC CCCGGAGAAG CGCGCCGGGG TGCACGACGG TCACCTCAAG
 301 CGCGCCCCCA AGGTGTACTG CGGGGGGGAC GAGCGCGACG TCCTCCGCGT
 351 CGGGTCGGGC GGCTTCTGGC CGCGGCGCTC GCGCCTGTGG GGCGGCGTGG
 401 ACCACGCCCC GGCGGGGTTC AACCCCACCG TCACCGTCTT TCACGTGTAT
 451 GACATCCTGG AGAACGTGGA GCACGCGTAC GGCATGCGCG CGGCCCAGTT
 501 CCACGCGCGG TTTATGGACG CCATCACACC GACGGGGACC GTCATCACGC
 551 TCCTGGGCCT GACTCCGGAA GGCCACCGGG TGGCCGTTCA CGTTTACGGC
 601 ACGCGGCAGT ACTTTTACAT GAACAAGGAG GAGGTTGACA GGCACCTACA
 651 ATGCCGCGCC CCACGAGATC TCTGCGAGCG CATGGCCGCG GCCCTGCGCG
 701 AGTCCCCGGG CGCGTCGTTC CGCGGCATCT CCGCGGACCA CTTCGAGGCG
 751 GAGGTGGTGG AGCGCACCGA CGTGTACTAC TACGAGACGC GCCCCGCTCT
 801 GTTTTACCGC GTCTACGTCC GAAGCGGGCG CGTGCTGTCG TACCTGTGCG
 851 ACAACTTCTG CCCGGCCATC AAGAAGTACG AGGGTGGGGT CGACGCCACC
 901 ACCCGGTTCA TCCTGGACAA CCCCGGGTTC GTCACCTTCG GCTGGTACCG
 951 TCTCAAACCG GGCCGGAACA ACACGCTAGC CCAGCCGCGG GCCCCGATGG
1001 CCTTCGGGAC ATCCAGCGAT GTCGAGTTTA ACTGTACGGC GGACAACCTG
1051 GCCATCGAGG GGGGCATGAG CGACCTACCG GCATACAAGC TCATGTGCTT
1101 CGATATCGAA TGCAAGGCGG GGGGGGAGGA CGAGCTGGCC TTTCCGGTGG
1151 CCGGGCACCC GGAGGACCTG GTCATCCAGA TATCCTGTCT GCTCTACGAC
1201 CTGTCCACCA CCGCCCTGGA GCACGTCCTC CTGTTTTCGC TCGGTTCCTG
1251 CGACCTCCCC GAATCCCACC TGAACGAGCT GGCGGCCAGG GGCCTGCCCA
1301 CGCCCGTGGT TCTGGAATTC GACAGCGAAT TCGAGATGCT GTTGGCCTTC
1351 ATGACCCTTG TGAAACAGTA CGGCCCCGAG TTCGTGACCG GGTACAACAT
1401 AATCAACTTC GACTGGCCCT TCTTGCTGGC CAAGCTGACG GACATTTACA
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1451 AGGTCCCCCT GGACGGGTAC GGCCGCATGA ACGGCCGGGG CGTGTTTCGC

1501 GTGTGGGACA TAGGCCAGAG CCACTTCCAG AAGCGCAGCA AGATAAAGGT

1551 GAACGGCATG GTGAACATCG ACATGTACGG GATTATAACC GACAAGATCA

1601 AGCTCTCGAG CTACAAGCTC AACGCCGTGG CCGAAGCCGT CCTGAAGGAC

1651 AAGAAGAAGG ACCTGAGCTA TCGCGACATC CCCACCTACT ACGCCGCCGG

1701 GCCCGCGCAA CGCGGGGTGA TCGGCGAGTA CTGCATACAG GATTCCCTGC

1751 TGGTGGGCCA GCTGTTTTTT AAGTTTTTGC CCCATCTGGA GCTCTCGGCC

1801 GTCGCGCGCT TGGCGGGTAT TAACATCACC CGCACCATCT ACGACGGCCA

1851 GCAGATCCGC GTCTTTACGT GCCTGCTGCG CCTGGCCGAC CAGAAGGGCT

1901 TTATTCTGCC GGACACCCAG GGGCGATTTA GGGGCGCCGG GGGGGAGGCG

1951 CCCAAGCGTC CGGCCGCAGC CCGGGAGGAC GAGGAGCGGC CAGAGGAGGA

2001 GGGGGAGGAC GAGAACGAAC GCGAGGAGGG CGGGGGCGAG CGGGAGCCGG

2051 AGGGCGCGCG GGAGACCGCC GGCCGGCACG TGGGGTACCA GGGGGCCAGG

2101 GTCCTTGACC CCACTTCCGG GTTTCACGTG AACCCCGTGG TGGTGTTCGA

2151 CTTTGCCAGC CTGTACCCCA GCATCATCCA GGCCCACAAC CTGTGCTTCA

2201 GCACGCTCTC CCTGAGGGCC GACGCAGTGG CGCACCTGGA GGCGGGCAAG

2251 GACTACCTGG AGATCGAGGT GGGGGGGCGA CGGCTGTTCT TCGTCAAGGC

2301 TCACGTGCGA GAGAGCCTCC TCAGCATCCT CCTGCGGGAC TGGCTCGCCA

2351 TGCGAAAGCA GATCCGCTCG CGGATTCCCC AGAGCAGCCC CGAGGAGGCC

2401 GTGCTCCTGG ACAAGCAGCA GGCCGCCATC AAGGTCGTGT GTAACTCGGT

2451 TTACGGGTTC ACGGGAGCGC AGCACGGACT CCTGCCGTGC CTGCACGTTG

2501 CCGCGACGGT GACGACCATC GGCCGCGAGA TGCTGCTCGC GACCCGCGAG

2551 TACGTCCACG CGCGCTGGGC GGCCTTCGAA CAGCTCCTGG CCGATTTCCC

2601 GGAGGCGGCC GACATGCGCG CCCCCGGGCC CTATTCCATG CGCATCATCT

2651 ACGGGGACAC GGACTCCATA TTTGTGCTGT GCCGCGGCCT CACGGCCGCC

2701 GGGCTGACGG CCGTGGGCGA CAAGATGGCG AGCCACATCT CGCGCGCGCT

2751 GTTTCTGCCC CCCATCAAAC TCGAGTGCGA AAAGACGTTC ACCAAGCTGC

2801 TGCTGATCGC CAAGAAAAAG TACATCGGCG TCATCTACGG GGGTAAGATG

2851 CTCATCAAGG GCGTGGATCT GGTGCGCAAA AACAACTGCG CGTTTATCAA

2901 CCGCACCTCC AGGGCCCTGG TCGACCTGCT GTTTTACGAC GATACCGTAT

2951 CCGGAGCGGC CGCCGCGTTA GCCGAGCGCC CCGCAGAGGA GTGGCTGGCG

3001 CGACCCCTGC CCGAGGGACT GCAGGCGTTC GGGGCCGTCC TCGTAGACGC

3051 CCATCGGCGC ATCACCGACC CGGAGAGGGA CATCCAGGAC TTTGTTCTCA

3101 CCGCCGAACT GAGCAGACAC CCGCGCGCGT ACACCAACAA GCGCCTGGCC

3151 CACCTGACGG TGTATTACAA GCTCATGGCC CGCCGCGCGC AGGTCCCGTC

3201 CATCAAGGAC CGGATCCCGT ACGTGATCGT GGCCCAGACC CGCGAGGTAG

3251 AGGAGACGGT CGCGCGGCTG GCCGCCCTCC GCGAGCTAGA CGCCGCCGCC

3301 CCAGGGGACG AGCCCGCCCC CCCCGCGGCC CTGCCCTCCC CGGCCAAGCG

3351 CCCCCGGGAG ACGCCGTCGC CTGCCGACCC CCCGGGAGGC GCGTCCAAGC

3401 CCCGCAAGCT GCTGGTGTCC GAGCTGGCCG AGGATCCCGC ATACGCCATT

3451 GCCCACGGCG TCGCCCTGAA CACGGACTAT TACTTCTCCC ACCTGTTGGG

3501 GGCGGCGTGC GTGACATTCA AGGCCCTGTT TGGGAATAAC GCCAAGATCA

3551 CCGAGAGTCT GTTAAAAAGG TTTATTCCCG AAGTGTGGCA CCCCCCGGAC

3601 GACGTGGCCG CGCGGCTCCG GACCGCAGGG TTCGGGGCGG TGGGTGCCGG

3651 CGCTACGGCG GAGGAAACTC GTCGAATGTT GCATAGAGCC TTTGATACTC

3701 TAGCATGA

SEQ.ID.NO. 10   Amino acid sequence of DNA polymerase for HSV1-DJL-M1

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   1 MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGRGPPPCL RQNFYNPYLA
  51 PVGTQQKPTG PTQRHTYYSE CDEFRFIAPR VLDEDAPPEK RAGVHDGHLK
 101 RAPKVYCGGD ERDVLRVGSG GFWPRRSRLW GGVDHAPAGF NPTVTVFHVY
 151 DILENVEHAY GMRAAQFHAR FMDAITPTGT VITLLGLTPE GHRVAVHVYG
 201 TRQYFYMNKE EVDRHLQCRA PRDLCERMAA ALRESPGASF RGISADHFEA
 251 EVVERTDVYY YETRPALFYR VYVRSGRVLS YLCDNFCPAI KKYEGGVDAT
 301 TRFILDNPGF VTFGWYRLKP GRNNTLAQPR APMAFGTSSD VEFNCTADNL
 351 AIEGGMSDLP AYKLMCFDIE CKAGGEDELA FPVAGHPEDL VIQISCLLYD
 401 LSTTALEHVL LFSLGSCDLP ESHLNELAAR GLPTPVVLEF DSEFEMLLAF
 451 MTLVKQYGPE FVTGYNIINF DWPFLLAKLT DIYKVPLDGY GRMNGRGVFR
 501 VWDIGQSHFQ KRSKIKVNGM VNIDMYGIIT DKIKLSSYKL NAVAEAVLKD
 551 KKKDLSYRDI PTYYAAGPAQ RGVIGEYCIQ DSLLVGQLFF KFLPHLELSA
 601 VARLAGINIT RTIYDGQQIR VFTCLLRLAD QKGFILPDTQ GRFRGAGGEA
 651 PKRPAAARED EERPEEEGED ENEREEGGGE REPEGARETA GRHVGYQGAR
 701 VLDPTSGFHV NPVVVFDFAS LYPSIIQAHN LCFSTLSLRA DAVAHLEAGK
 751 DYLEIEVGGR RLFFVKAHVR ESLLSILLRD WLAMRKQIRS RIPQSSPEEA
 801 VLLDKQQAAI KVVCNSVYGF TGAQHGLLPC LHVAATVTTI GREMLLATRE
 851 YVHARWAAFE QLLADFPEAA DMRAPGPYSM RIIYGDTDSI FVLCRGLTAA
 901 GLTAVGDKMA SHISRALFLP PIKLECEKTF TKLLLIAKKK YIGVIYGGKM
 951 LIKGVDLVRK NNCAFINRTS RALVDLLFYD DTVSGAAAAL AERPAEEWLA
1001 RPLPEGLQAF GAVLVDAHRR ITDPERDIQD FVLTAELSRH PRAYTNKRLA
1051 HLTVYYKLMA RRAQVPSIKD RIPYVIVAQT REVEETVARL AALRELDAAA
1101 PGDEPAPPAA LPSPAKRPRE TPSPADPPGG ASKPRKLLVS ELAEDPAYAI
1151 AHGVALNTDY YFSHLLGAAC VTFKALFGNN AKITESLLKR FIPEVWHPPD
1201 DVAARLRTAG FGAVGAGATA EETRRMLHRA FDTLA*
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SEQ.ID.NO. 11   DNA sequence of DNA polymerase gene for HMCV-AD169-M1

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   1 ATGTTTTTCA ACCCGTATCT GAGCGGCGGC GTGACCGGCG GTGCGGTCGC

  51 GGGTGGCCGG CGTCAGCGTT CGCAGCCCGG CTCCGCGCAG GGCTCGGGCA

 101 AGCGGCCGCC ACAGAAACAG TTTTTGCAGA TCGTGCCGCG AGGTGTCATG

 151 TTCGACGGTC AGACGGGGTT GATCAAGCAT AAGACGGGAC GGCTGCCTCT

 201 CATGTTCTAT CGAGAGATTA AACATTTGTT GAGTCATGAC ATGGTTTGGC

 251 CGTGTCCTTG GCGCGAGACC CTGGTGGGTC GCGTGGTGGG ACCTATTCGT

 301 TTTCACACCT ACGATCAGAC GGACGCCGTG CTCTTCTTCG ACTCGCCCGA

 351 AAACGTGTCG CCGCGCTATC GTCAGCATCT GGTGCCTTCG GGGAACGTGT

 401 TGCGTTTCTT CGGGGCCACA GAACACGGCT ACAGTATCTG CGTCAACGTT

 451 TTCGGGCAGC GCAGCTACTT TTACTGTGAG TACAGCGACA CCGATAGGCT

 501 GCGTGAGGTC ATTGCCAGCG TGGGCGAACT AGTGCCCGAA CCGCGGACGC

 551 CATACGCCGT GTCTGTCACG CCGGCCACCA AGACCTCCAT CTATGGGTAC

 601 GGGACGCGAC CCGTGCCCGA TTTGCAGTGT GTGTCTATCA GCAACTGGAC

 651 CATGGCCAGA AAAATCGGCG AGTATCTGCT GGAGCAGGGT TTTCCCGTGT

 701 ACGAGGTCCG TGTGGATCCG CTGACGCGTT TGGTCATCGA TCGGCGGATC

 751 ACCACGTTCG GCTGGTGCTC CGTGAATCGT TACGACTGGC GGCAGCAGGG

 801 TCGCGCGTCG ACTTGTGATA TCGAGGTAGA CTGCGATGTC TCTGACCTGG

 851 TGGCTGTGCC CGACGACAGC TCGTGGCCGC GCTATCGATG CCTGTCCTTC

 901 GATATCGAGT GCATGAGCGG CGAGGGTGGT TTTCCCTGCG CCGAGAAGTC

 951 CGATGACATT GTCATTCAGA TCTCGTGCGT GTGCTACGAG ACGGGGGGAA

1001 ACACCGCCGT GGATCAGGGG ATCCCAAACG GGAACGATGG TCGGGGCTGC

1051 ACTTCGGAGG GTGTGATCTT TGGGCACTCG GGTCTTCATC TCTTTACGAT

1101 CGGCACCTGC GGGCAGGTGG CCCAGACGT GGACGTCTAC GAGTTCCCTT

1151 CCGAATACGA GCTGCTGCTG GGCTTTATGC TTTTCTTTCA ACGGTACGCG

1201 CCGGCCTTTG TGACCGGTTA CAACATCAAC TCTTTTGACT TGAAGTACAT

1251 CCTCACGCGT CTCGAGTACC TGTATAAGGT GGACTCGCAG CGCTTCTGCA

1301 AGTTGCCTAC GGCGCAGGGC GGCCGTTTCT TTTTACACAG CCCCGCCGTG

1351 GGTTTTAAGC GGCAGTACGC CGCCGCTTTT CCCTCGGCTT CTCACAACAA

1401 TCCGGCCAGC ACGGCCGCCA CCAAGGTGTA TATTGCGGGT TCGGTGGTTA
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1451 TCGACATGTA CCCTGTATGC ATGGCCAAGA CTAACTCGCC CAACTATAAG

1501 CTCAACACTA TGGCCGAGCT TTACCTGCGG CAACGCAAGG ATGACCTGTC

1551 TTACAAGGAC ATCCCGCGTT GTTTCGTGGC TAATGCCGAG GGCCGCGCCC

1601 AGGTAGGCCG TTACTGTCTG CAGGACGCCG TATTGGTGCG CGATCTGTTC

1651 AACACCATTA ATTTTCACTA CGAGGCCGGG GCCATCGCGC GGCTGGCTAA

1701 AATTCCGTTG CGGCGTGTCA TCTTTGACGG ACAGCAGATC CGTATCTACA

1751 CCTCGCTGCT GGACGAGTGC GCCTGCCGCG ATTTTATCCT GCCCAACCAC

1801 TACAGCAAAG GTACGACGGT GCCCGAAACG AATAGCGTTG CTGTGTCACC

1851 TAACGCTGCT ATCATCTCTA CCGCCGCTGT GCCCGGCGAC GCGGGTTCTG

1901 TGGCGGCTAT GTTTCAGATG TCGCCGCCCT TGCAATCTGC GCCGTCCAGT

1951 CAGGACGGCG TTTCACCCGG CTCCGGCAGT AACAGTAGTA GCAGCGTCGG

2001 CGTTTTCAGC GTCGGCTCCG GCAGTAGTGG CGGCGTCGGC GTTTCCAACG

2051 ACAATCACGG CGCCGGCGGT ACTGCGGCGG TTTCGTACCA GGGCGCCACG

2101 GTGTTTGAGC CCGAGGTGGG TTACTACAAC GACCCCGTGG CCGTGTTCGA

2151 CTTTGCCAGC CTCTACCCTT CCATCATCAT GGCCCACAAC CTCTGCTACT

2201 CCACCCTGCT GGTGCCGGGT GGCGAGTACC CTGTGGACCC CGCCGACGTA

2251 TACAGCGTCA CGCTAGAGAA CGGCGTGACC CACCGCTTTG TGCGTGCTTC

2301 GGTGCGCGTC TCGGTGCTCT CGGAACTGCT CAACAAGTGG GTTTCGCAGC

2351 GGCGTGCCGT GCGCGAATGC ATGCGCGAGT GTCAAGACCC TGTGCGCCGT

2401 ATGCTGCTCG ACAAGGAACA GATGGCGCTC AAAGTAACGT GCAACGCTTT

2451 CTACGGTTTT ACCGGCGCGC TGAACGGTAT GATGCCGTGT CTGCCCATCG

2501 CCGCCAGCAT CACGCGCATC GGTCGCGACA TGCTAGAGCG CACGGCGCGG

2551 TTCATCAAAG ACAACTTTTC AGAGCCGTGT TTTTTGCACA ATTTTTTTAA

2601 TCAGGAAGAC TATGTAGTGG AACGCGGGA GGGGGATTCG GAGGAGAGCA

2651 GCGCGTTACC GGAGGGGCTC GAAACATCGT CAGGGGGCTC GAACGAACGG

2701 CGGGTGGAGG CGCGGGTCAT CTACGGGGAC ACGGACAGCG TGTTTGTCCG

2751 CTTTCGTGGC CTGACGCCGC AGGCTCTGGT GGCGCGTGGG CCCAGCCTGG

2801 CGCACTACGT GACGGCCTGT CTTTTTGTGG AGCCCGTCAA GCTGGAGTTT

2851 GAAAAGGTCT TCGTCTCTCT TATGATGATC TGCAAGAAAC GTTACATCGG

2901 CAAAGTGGAG GGCGCCTCGG GTCTGAGCAT GAAGGGCGTG GATCTGGTGC

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3301 CTGACGGCGC CCGGTGTCCG GACGGCGCCG CAGGGTTCCT CCGACAACGG

3351 TGATTCTGTA ACCGCCGGCG TGGTTTCCCG GTCGGACGCG ATTGATGGCA

3401 CGGACGACGA CGCTGACGGC GGCGGGGTAG AGGAGAGCAA CAGGAGAGGA

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3601 CTGTCGCCCG TCTTTCCCGG CGGCGAAACC GCGCGCAAGG ACAAGTTTTT

3651 GCACATGGTG CTGCCGCGGC GCTTGCACTT GGAGCCGGCT TTTCTGCCGT

3701 ACAGTGTCAA GGCGCACGAA TGCTGTTGA

SEQ.ID.NO.12   Amino acid sequence of DNA polymerase for HCMV-AD169-M1

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  1 MFFNPYLSGG VTGGAVAGGR RQRSQPGSAQ GSGKRPPQKQ FLQIVPRGVM

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101 FHTYDQTDAV LFFDSPENVS PRYRQHLVPS GNVLRFFGAT EHGYSICVNV

151 FGQRSYFYCE YSDTDRLREV IASVGELVPE PRTPYAVSVT PATKTSIYGY

201 GTRPVPDLQC VSISNWTMAR KIGEYLLEQG FPVYEVRVDP LTRLVIDRRI

251 TTFGWCSVNR YDWRQQGRAS TCDIEVDCDV SDLVAVPDDS SWPRYRCLSF

301 DIECMSGEGG FPCAEKSDDI VIQISCVCYE TGGNTAVDQG IPNGNDGRGC

351 TSEGVIFGHS GLHLFTIGTC GQVGPDVDVY EFPSEYELLL GFMLFFQRYA

401 PAFVTGYNIN SFDLKYILTR LEYLYKVDSQ RFCKLPTAQG GRFFLHSPAV

451 GFKRQYAAAF PSASHNNPAS TAATKVYIAG SVVIDMYPVC MAKTNSPNYK

501 LNTMAELYLR QRKDDLSYKD IPRCFVANAE GRAQVGRYCL QDAVLVRDLF

551 NTINFHYEAG AIARLAKIPL RRVIFDGQQI RIYTSLLDEC ACRDFILPNH

601 YSKGTTVPET NSVAVSPNAA IISTAAVPGD AGSVAAMFQM SPPLQSAPSS

651 QDGVSPGSGS NSSSSVGVFS VGSGSSGGVG VSNDNHGAGG TAAVSYQGAT

701 VFEPEVGYYN DPVAVFDFAS LYPSIIMAHN LCYSTLLVPG GEYPVDPADV

751 YSVTLENGVT HRFVRASVRV SVLSELLNKW VSQRRAVREC MRECQDPVRR

801 MLLDKEQMAL KVTCNAFYGF TGALNGMMPC LPIAASITRI GRDMLERTAR

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1051 VRVEDLVLSS VLSKDISLYR QSNLPHIAVI KRLAARSEEL PSVGDRVFYV

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1151 GEPAKKRARK PPSAVCNYEV AEDPSYVREH GVPIHADKYF EQVLKAVTNV

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Figure 6
SEQ.ID.NO.13   Amino acid sequence of DNA polymerase for HCMV-AD169

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10   151 FGQRSYFYCE YSDTDRLREV IASVGELVPE PRTPYAVSVT PATKTSIYGY

     201 GTRPVPDLQC VSISNWTMAR KIGEYLLEQG FPVYEVRVDP LTRLVIDRRI

15   251 TTFGWCSVNR YDWRQQGRAS TCDIEVDCDV SDLVAVPDDS SWPRYRCLSF

     301 DIECMSGEGG FPCAEKSDDI VIQISCVCYE TGGNTAVDQG IPNGNDGRGC

     351 TSEGVIFGHS GLHLFTIGTC GQVGPDVDVY EFPSEYELLL GFMLFFQRYA

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25   501 LNTMAELYLR QRKDDLSYKD IPRCFVANAE GRAQVGRYCL QDAVLVRDLF

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30   651 QDGVSPGSGS NSSSSVGVFS VGSGSSGGVG VSNDNHGAGG TAAVSYQGAT

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35   751 YSVTLENGVT HRFVRASVRV SVLSELLNKW VSQRRAVREC MRECQDPVRR

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50 1151 GEPAKKRARK PPSAVCNYEV AEDPSYVREH GVPIHADKYF EQVLKAVTNV

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SEQUENCE LISTING

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Gln Gly Arg Phe Arg Gly Leu Asp Lys Glu Ala Pro Lys Arg Pro Ala
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acggagatct acaaggtccc gctcgacggg tacgggcgca tgaacggccg gggtgtgttc   1500

cgcgtgtggg acatcggcca gagccacttt cagaagcgca gcaagatcaa ggtgaacggg   1560

atggtgaaca tcgacatgta cggcatcatc accgacaagg tcaaactctc cagctacaag   1620

ctgaacgccg tcgccgaggc cgtcttgaag gacaagaaga aggatctgag ctaccgcgac   1680

atccccgcct actacgcctc cgggcccgcg cagcgcgggg tgatcggcga gtattgtgtg   1740

caggactcgc tgctggtcgg gcagctgttc ttcaagtttc tgccgcacct ggagctttcc   1800

gccgtcgcgc gcctggcggg catcaacatc acccgcacca tctacgacgg ccagcagatc   1860

cgcgtcttca cgtgcctcct gcgccttgcg ggccagaagg gcttcatcct gccggacacc   1920

caggggcggt ttcgggggcct cgacaaggag gcgcccaagc gcccggccgt gcctcggggg   1980

gaaggggagc ggccgggggga cgggaacggg gacgaggata aggacgacga cgaggacggg   2040

gacgaggacg gggacgagcg cgaggaggtc gcgcgcgaga ccggggggccg gcacgttggg   2100

taccaggggg cccgggtcct cgaccccacc tccgggtttc acgtcgaccc cgtggtggtg   2160

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ccccccgagg aggccgtcct cctcgacaag caacaggccg ccatcaaggt ggtgtgcaac   2460

tcggtgtacg ggttcaccgg ggcgcagcac ggtcttctgc cctgcctgca cgtggccgcc   2520

accgtgacga ccatcggccg cgagatgctc ctcgcgacgc gcgcgtacgt gcacgcgcgc   2580

tgggcggagt tcgatcagct gctggccgac tttccggagg cggccggcat gcgcgccccc   2640

ggtccgtact ccatgcgcat catctacggg gacacggact ccattttcgt tttgtgccgc   2700

ggcctcacgg ccgcgggcct ggtggccatg ggcgacaaga tggcgagcca catctcgcgc   2760

gcgctgttcc tcccccccgat caagctcgag tgcgaaaaaa cgttcaccaa gctgctgctc   2820

atcgccaaga aaaagtacat cggcgtcatc tgcggggggca agatgctcat caagggcgtg   2880

gatctggtgc gcaaaaacaa ctgcgcgttt atcaaccgca cctccagggc cctggtcgac   2940

ctgctgtttt acgacgatac cgtatccgga gcggccgccg cgttagccga gcgccccgca   3000

8

```
gaggagtggc tggcgcgacc cctgcccgag ggactgcagg cgttcggggc cgtcctcgta    3060

gacgcccatc ggcgcatcac cgacccggag agggacatcc aggactttgt cctcaccgcc    3120

gaactgagca gacacccgcg cgcgtacacc aacaagcgcc tggcccacct gacggtgtat    3180

tacaagctca tggcccgccg cgcgcaggtc ccgtccatca aggaccggat cccgtacgtg    3240

atcgtggccc agacccgcga ggtagaggag acggtcgcgc ggctggccgc cctccgcgag    3300

ctagacgccg ccgccccagg ggacgagccc gcccccccag cggccctgcc ctccccggcc    3360

aagcgccccc gggagacgcc gtcgcatgcc gaccccccgg gaggcgcgtc caagccccgc    3420

aagctgctgg tgtccgagct ggcggaggat cccgggtacg ccatcgcccg gggcgttccg    3480

ctcaacacgg actattactt ctcgcacctg ctggggggcgg cctgcgtgac gttcaaggcc    3540

ctgtttggaa ataacgccaa gatcaccgag agtctgttaa agaggtttat tcccgagacg    3600

tggcacccccc cggacgacgt ggccgcgcgg ctcagggccg cggggttcgg gccggcgggg    3660

gccggcgcta cggcggagga aactcgtcga atgttgcata gagcctttga tactctagca    3720

tga                                                                  3723
```

<210>   4
<211>   1240
<212>   PRT
<213>   herpes simplex

<400>   4

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Met Phe Cys Ala Ala Gly Gly Pro Ala Ser Pro Gly Gly Lys Ser Ala
1               5                   10                  15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro His Asn Pro Arg Gly Ala
            20                  25                  30

Thr Gln Thr Ala Pro Pro Pro Cys Arg Arg Gln Asn Phe Tyr Asn Pro
        35                  40                  45

His Leu Ala Gln Thr Gly Thr Gln Pro Lys Ala Pro Gly Pro Ala Gln
    50                  55                  60

Arg His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro
65                  70                  75                  80

Arg Ser Leu Asp Glu Asp Ala Pro Ala Glu Gln Arg Thr Gly Val His
            85                  90                  95

Asp Gly Arg Leu Arg Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu
            100                 105                 110

Arg Asp Val Leu Arg Val Gly Pro Glu Gly Phe Trp Pro Arg Arg Leu
            115                 120                 125

Arg Leu Trp Gly Gly Ala Asp His Ala Pro Glu Gly Phe Asp Pro Thr
    130                 135                 140

Val Thr Val Phe His Val Tyr Asp Ile Leu Glu His Val Glu His Ala
```

```
145                 150                 155                 160

Tyr Ser Met Arg Ala Ala Gln Leu His Glu Arg Phe Met Asp Ala Ile
            165             170             175

Thr Pro Ala Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly
            180             185             190

His Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met
            195             200             205

Asn Lys Ala Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp
    210             215             220

Leu Cys Glu Arg Leu Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser
225             230             235             240

Phe Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg
            245             250             255

Ala Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Thr Leu Tyr Tyr Arg Val
            260             265             270

Phe Val Arg Ser Gly Arg Ala Leu Ala Tyr Leu Cys Asp Asn Phe Cys
            275             280             285

Pro Ala Ile Arg Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe
    290             295             300

Ile Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys
305             310             315             320

Pro Gly Arg Gly Asn Ala Pro Ala Gln Pro Arg Pro Pro Thr Ala Phe
            325             330             335

Gly Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala
            340             345             350

Val Glu Gly Ala Met Cys Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe
            355             360             365

Asp Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val
    370             375             380

Ala Glu Arg Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr
385             390             395             400

Asp Leu Ser Thr Thr Ala Leu Glu His Ile Leu Leu Phe Ser Leu Gly
            405             410             415

Ser Cys Asp Leu Pro Glu Ser His Leu Ser Asp Leu Ala Ser Arg Gly
            420             425             430

Leu Pro Ala Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu
            435             440             445

Leu Ala Phe Met Thr Phe Val Lys Gln Tyr Gly Pro Glu Phe Val Thr
    450             455             460

Gly Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Val Leu Thr Lys Leu
465             470             475             480
```

10

```
Thr Glu Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly
             485                 490                 495

Arg Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys
             500                 505                 510

Arg Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly
             515                 520                 525

Ile Ile Thr Asp Lys Val Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val
         530                 535                 540

Ala Glu Ala Val Leu Lys Asp Lys Lys Lys Asp Leu Ser Tyr Arg Asp
545                 550                 555                 560

Ile Pro Ala Tyr Tyr Ala Ser Gly Pro Ala Gln Arg Gly Val Ile Gly
             565                 570                 575

Glu Tyr Cys Val Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys
             580                 585                 590

Phe Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile
             595                 600                 605

Asn Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr
         610                 615                 620

Cys Leu Leu Arg Leu Ala Gly Gln Lys Gly Phe Ile Leu Pro Asp Thr
625                 630                 635                 640

Gln Gly Arg Phe Arg Gly Leu Asp Lys Glu Ala Pro Lys Arg Pro Ala
             645                 650                 655

Val Pro Arg Gly Glu Gly Glu Arg Pro Gly Asp Gly Asn Gly Asp Glu
             660                 665                 670

Asp Lys Asp Asp Asp Glu Asp Gly Asp Glu Asp Gly Asp Glu Arg Glu
         675                 680                 685

Glu Val Ala Arg Glu Thr Gly Gly Arg His Val Gly Tyr Gln Gly Ala
         690                 695                 700

Arg Val Leu Asp Pro Thr Ser Gly Phe His Val Asp Pro Val Val Val
705                 710                 715                 720

Phe Asp Phe Ala Ser Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu
             725                 730                 735

Cys Phe Ser Thr Leu Ser Leu Arg Pro Glu Ala Val Ala His Leu Glu
             740                 745                 750

Ala Asp Arg Asp Tyr Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe
         755                 760                 765

Phe Val Lys Ala His Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg
         770                 775                 780

Asp Trp Leu Ala Met Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser
785                 790                 795                 800

Pro Pro Glu Glu Ala Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys
             805                 810                 815
```

11

```
Val Val Cys Asn Ser Val Tyr Gly Phe Thr Gly Ala Gln His Gly Leu
        820                 825                 830

Leu Pro Cys Leu His Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu
        835                 840                 845

Met Leu Leu Ala Thr Arg Ala Tyr Val His Ala Arg Trp Ala Glu Phe
    850                 855                 860

Asp Gln Leu Leu Ala Asp Phe Pro Glu Ala Ala Gly Met Arg Ala Pro
865                 870                 875                 880

Gly Pro Tyr Ser Met Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe
            885                 890                 895

Val Leu Cys Arg Gly Leu Thr Ala Ala Gly Leu Val Ala Met Gly Asp
        900                 905                 910

Lys Met Ala Ser His Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys
    915                 920                 925

Leu Glu Cys Glu Lys Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys
    930                 935                 940

Lys Tyr Ile Gly Val Ile Cys Gly Gly Lys Met Leu Ile Lys Gly Val
945                 950                 955                 960

Asp Leu Val Arg Lys Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg
            965                 970                 975

Ala Leu Val Asp Leu Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala
            980                 985                 990

Ala Ala Leu Ala Glu Arg Pro Ala  Glu Glu Trp Leu Ala  Arg Pro Leu
        995                 1000                1005

Pro Glu  Gly Leu Gln Ala Phe  Gly Ala Val Leu Val  Asp Ala His
    1010                1015                1020

Arg Arg  Ile Thr Asp Pro Glu  Arg Asp Ile Gln Asp  Phe Val Leu
    1025                1030                1035

Thr Ala  Glu Leu Ser Arg His  Pro Arg Ala Tyr Thr  Asn Lys Arg
    1040                1045                1050

Leu Ala  His Leu Thr Val Tyr  Tyr Lys Leu Met Ala  Arg Arg Ala
    1055                1060                1065

Gln Val  Pro Ser Ile Lys Asp  Arg Ile Pro Tyr Val  Ile Val Ala
    1070                1075                1080

Gln Thr  Arg Glu Val Glu Glu  Thr Val Ala Arg Leu  Ala Ala Leu
    1085                1090                1095

Arg Glu  Leu Asp Ala Ala Ala  Pro Gly Asp Glu Pro  Ala Pro Pro
    1100                1105                1110

Ala Ala  Leu Pro Ser Pro Ala  Lys Arg Pro Arg Glu  Thr Pro Ser
    1115                1120                1125

His Ala  Asp Pro Pro Gly Gly  Ala Ser Lys Pro Arg  Lys Leu Leu
```

```
         1130                   1135                   1140
Val Ser Glu Leu Ala Glu Asp Pro Gly Tyr Ala Ile Ala Arg Gly
    1145                   1150                   1155

Val Pro Leu Asn Thr Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala
    1160                   1165                   1170

Ala Cys Val Thr Phe Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile
    1175                   1180                   1185

Thr Glu Ser Leu Leu Lys Arg Phe Ile Pro Glu Thr Trp His Pro
    1190                   1195                   1200

Pro Asp Asp Val Ala Ala Arg Leu Arg Ala Ala Gly Phe Gly Pro
    1205                   1210                   1215

Ala Gly Ala Gly Ala Thr Ala Glu Glu Thr Arg Arg Met Leu His
    1220                   1225                   1230

Arg Ala Phe Asp Thr Leu Ala
    1235                   1240
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<210> 5
<211> 3708
<212> DNA
<213> herpes simplex

<400> 5

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aggcaaaact tttacaaccc ctacctcgcc ccagtcggga cgcaacagaa gccgaccggg   180

ccaacccagc gccatacgta ctatagcgaa tgcgatgaat ttcgattcat cgccccgcgg   240

gtgctggacg aggatgcccc cccggagaag cgcgccgggg tgcacgacgg tcacctcaag   300

cgcgccccca aggtgtactg cgggggggac gagcgcgacg tcctccgcgt cgggtcgggc   360

ggcttctggc cgcggcgctc gcgcctgtgg ggcggcgtgg accacgcccc ggcggggttc   420

aaccccaccg tcaccgtctt tcacgtgtac gacatcctgg agaacgtgga gcacgcgtac   480

ggcatgcgcg cggcccagtt ccacgcgcgg tttatggacg ccatcacacc gacggggacc   540

gtcatcacgc tcctgggcct gactccggaa ggccaccggg tggccgttca cgtttacggc   600

acgcggcagt actttttacat gaacaaggag gaggttgaca ggcacctaca atgccgcgcc   660

ccacgagatc tctgcgagcg catggccgcg gccctgcgcg agtccccggg cgcgtcgttc   720

cgcggcatct ccgcggacca cttcgaggcg gaggtggtgg agcgcaccga cgtgtactac   780

tacgagacgc gccccgctct gttttaccgc gtctacgtcc gaagcgggcg cgtgctgtcg   840

tacctgtgcg acaacttctg cccggccatc aagaagtacg agggtggggt cgacgccacc   900

acccggttca tcctggacaa ccccgggttc gtcaccttcg gctggtaccg tctcaaaccg   960

ggccggaaca acacgctagc ccagccgcgg gccccgatgg ccttcgggac atccagcgac  1020
```

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gtcgagttta actgtacggc ggacaacctg gccatcgagg ggggcatgag cgacctaccg      1080

gcatacaagc tcatgtgctt cgatatcgaa tgcaaggcgg ggggggagga cgagctggcc      1140

tttccggtgg ccgggcaccc ggaggacctg gttattcaga tatcctgtct gctctacgac      1200

ctgtccacca ccgccctgga gcacgtcctc ctgttttcgc tcggttcctg cgacctcccc      1260

gaatcccacc tgaacgagct ggcggccagg ggcctgccca cgcccgtggt tctggaattc      1320

gacagcgaat tcgagatgct gttggccttc atgacccttg tgaaacagta cggccccgag      1380

ttcgtgaccg ggtacaacat catcaacttc gactggccct tcttgctggc caagttgacg      1440

gacatttaca aggtcccccct ggacgggtac ggccgcatga acggccgggg cgtgtttcgc      1500

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gtgaacatcg acatgtacgg gatcataacc gacaagatca agctctcgag ctacaagctc      1620

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gtctttacgt gcctgctgcg cctggccgac cagaagggct ttattctgcc ggacacccag      1920

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cgggagccgg agggcgcgcg ggagaccgcc ggccggcacg tggggtacca gggggccagg      2100

gtccttgacc ccacttccgg gtttcacgtg aaccccgtgg tggtgttcga ctttgccagc      2160

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gggctgacgg ccatgggcga caagatggcg agccacatct cgcgcgcgct gtttctgccc      2760

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gacgtggccg cgcggctccg ggccgcaggg ttcggggcgg tgggtgccgg cgctacggcg   3660

gaggaaactc gtcgaatgtt gcatagagcc tttgatactc tagcatga             3708
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<210>  6
<211>  1235
<212>  PRT
<213>  herpes simplex

<400>  6

Met Phe Ser Gly Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala
1               5                  10                  15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala
            20                  25                  30

Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr
        35                  40                  45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg
    50                  55                  60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg
65                  70                  75                  80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp
                85                  90                  95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg
            100                 105                 110

Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg
        115                 120                 125

Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val
```

```
              130                  135                     140

    Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr
    145             150                 155                 160

    Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr
                    165                 170                 175

    Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His
                180                 185                 190

    Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn
            195                 200                 205

    Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu
    210                 215                 220

    Cys Glu Arg Met Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe
    225                 230                 235                 240

    Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr
                    245                 250                 255

    Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr
                260                 265                 270

    Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro
            275                 280                 285

    Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile
        290                 295                 300

    Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro
    305                 310                 315                 320

    Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly
                    325                 330                 335

    Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile
                340                 345                 350

    Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp
            355                 360                 365

    Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala
        370                 375                 380

    Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp
    385                 390                 395                 400

    Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser
                    405                 410                 415

    Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu
                420                 425                 430

    Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu
            435                 440                 445

    Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly
        450                 455                 460
```

```
Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Leu Leu Ala Lys Leu Thr
465             470             475             480

Asp Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly Arg
            485             490             495

Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys Arg
        500             505             510

Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly Ile
    515             520             525

Ile Thr Asp Lys Ile Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val Ala
    530             535             540

Glu Ala Val Leu Lys Asp Lys Lys Asp Leu Ser Tyr Arg Asp Ile
545             550             555             560

Pro Ala Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu
        565             570             575

Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe
        580             585             590

Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn
        595             600             605

Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys
    610             615             620

Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln
625             630             635             640

Gly Arg Phe Arg Gly Ala Gly Gly Glu Ala Pro Lys Arg Pro Ala Ala
            645             650             655

Ala Arg Glu Asp Glu Glu Arg Pro Glu Glu Glu Gly Glu Asp Glu Asp
            660             665             670

Glu Arg Glu Glu Gly Gly Gly Glu Arg Glu Pro Glu Gly Ala Arg Glu
        675             680             685

Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro
    690             695             700

Thr Ser Gly Phe His Val Asn Pro Val Val Val Phe Asp Phe Ala Ser
705             710             715             720

Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu
            725             730             735

Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr
            740             745             750

Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His
        755             760             765

Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met
    770             775             780

Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala
785             790             795             800
```

Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser
              805   810   815

Val Tyr Gly Phe Thr Gly Ala Gln His Gly Leu Leu Pro Cys Leu His
              820   825   830

Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu Leu Ala Thr
              835   840   845

Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala
    850   855   860

Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met
865   870   875   880

Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly
              885   890   895

Leu Thr Ala Ala Gly Leu Thr Ala Met Gly Asp Lys Met Ala Ser His
              900   905   910

Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu Cys Glu Lys
        915   920   925

Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val
    930   935   940

Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys
945   950   955   960

Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu
              965   970   975

Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Ala Leu Ala Glu
        980   985   990

Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln
    995   1000   1005

Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg Ile Thr Asp
    1010   1015   1020

Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala Glu Leu Ser   - . ··   .
    1025   1030   1035

Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala His Leu Thr
    1040   1045   1050

Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val Pro Ser Ile
    1055   1060   1065

Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr Arg Glu Val
    1070   1075   1080

Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu Leu Asp Ala
    1085   1090   1095   :

Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala Leu Pro Ser   '   .
    1100   1105   1110

Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser His Ala Asp Pro Pro

```
     1115                      1120                     1125

Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu Val Ser Glu Leu Ala
    1130                    1135                 1140

Glu Asp Pro Ala Tyr Ala Ile Ala His Gly Val Ala Leu Asn Thr
    1145                    1150                 1155

Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala Ala Cys Val Thr Phe
    1160                    1165                 1170

Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile Thr Glu Ser Leu Leu
    1175                    1180                 1185

Lys Arg Phe Ile Pro Glu Val Trp His Pro Pro Asp Asp Val Ala
    1190                    1195                 1200

Ala Arg Leu Arg Ala Ala Gly Phe Gly Ala Val Gly Ala Gly Ala
    1205                    1210                 1215

Thr Ala Glu Glu Thr Arg Arg Met Leu His Arg Ala Phe Asp Thr
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Leu Ala
    1235
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aggcaaaact tttacaaccc ctacctcgcc ccagtcggga cgcaacagaa gccgaccggg   180

ccaacccagc gccatacgta ctatagcgaa tgcgatgaat ttcgattcat cgccccgcgg   240

gtgctggacg aggatgcccc cccggagaag cgcgccgggg tgcacgacgg tcacctcaag   300

cgcgccccca aggtgtactg cggggggggac gagcgcgacg tcctccgcgt cgggtcgggc   360

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gtcatcacgc tcctgggcct gactccggaa ggccaccggg tggccgttca cgtttacggc   600

acgcggcagt acttttacat gaacaaggag gaggtcgaca ggcacctaca atgccgcgcc   660

ccacgagatc tctgcgagcg catggccgcg gccctgcgcg agtccccggg cgcgtcgttc   720

cgcggcattt ccgcggacca cttcgaggcg gaggtggtgg agcgcaccga cgtgtactac   780

tacgagacgc gccccgctct gtttta ccgc gtctacgtcc gaagcgggcg cgtgctgtcg   840

tacctgtgcg acaacttctg cccggccatc aagaagtacg agggtggggt cgacgccacc   900
```

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gtcgagttta actgtacggc ggacaacctg gccatcgagg ggggcatgag cgacctaccg     1080

gcatacaagc tcatgtgctt cgatatcgaa tgcaaggcgg gggggggagga cgagctggcc    1140

tttccggtgg ccgggcaccc ggaggacctg gtcatccaga tatcctgtct gctctacgac     1200

ctgtccacca ccgccctgga gcacgtcctc ctgttttcgc tcggttcctg cgacctcccc     1260

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cggctgttct tcgtcaaggc tcacgtgcga gagagcctcc tcagcatcct cctgcgggac     2340

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acgggagcgc agcacggact cctgccgtgc ctgcacgttg ccgcgacggt gacgaccatc     2520

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cagctcctgg ccgatttccc ggaggcggcc gacatgcgcg cccccgggcc ctattccatg     2640

cgcatcatct acggggacac ggactccatc tttgtgctgt ccgcgcggcct cacggccgcc     2700

gggctgacgg ccgtgggcga caagatggcg agccacatct cgcgcgcgct gtttctgtcc     2760
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20

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cccatcaaac tcgagtgcga aaagacgttc accaagctgc tgctgatcgc caagaaaaag   2820

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aacaactgcg cgtttatcaa ccgcacctcc agggccctgg tcgacctgct gttttacgac   2940

gataccgtat ccggagcggc cgccgcgtta gccgagcgcc ccgcagagga gtggctggcg   3000

cgacccctgc ccgagggact gcaggcgttc ggggccgtcc tcgtagacgc ccatcggcgc   3060

atcaccgacc cggagaggga catccaggac tttgtcctca ccgccgaact gagcagacac   3120

ccgcgcgcgt acaccaacaa gcgcctggcc cacctgacgg tgtattacaa gctcatggcc   3180

cgccgcgcgc aggtcccgtc catcaaggac cggatcccgt acgtgatcgt ggcccagacc   3240

cgcgaggtag aggagacggt cgcgcggctg ccgccctcc gcgagctcga cgccgccgcc    3300

ccaggggacg agcccgcccc ccccgcggcc ctgccctccc cggccaagcg ccccgggag    3360

acgccgttgc atgccgaccc cccgggaggc gcgtccaagc cccgcaagct gctggtgtcc    3420

gagctggccg aggatcccgc atacgccatt gcccacggcg tcgccctgaa cacggactat    3480

tacttctccc acctgttggg ggcggcgtgc gtgacattca aggccctgtt tgggaataac    3540

gccaagatca ccgagagtct gttaaaaagg tttattcccg aagtgtggca cccccccggac   3600

gacgtggccg cgcggctccg ggccgcaggg ttcggggcgg tgggtgccgg cgctacggcg   3660

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<212>    PRT
<213>    herpes simplex

<400>    8

Met Phe Ser Gly Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala
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Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala
            20                  25                  30

Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr
        35                  40                  45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg
    50                  55                  60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg
65                  70                  75                  80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp
                85                  90                  95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg
            100                 105                 110

Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg
```

21

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              115                    120                    125

      Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val
          130                135                140

      Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr
      145                150                155                160

      Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr
                  165                170                175

      Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His
                  180                185                190

      Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn
              195                200                205

      Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu
          210                215                220

      Cys Glu Arg Met Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe
      225                230                235                240

      Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr
                  245                250                255

      Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr
                  260                265                270

      Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro
              275                280                285

      Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile
          290                295                300

      Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro
      305                310                315                320

      Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly
                  325                330                335

      Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile
                  340                345                350

      Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp
              355                360                365

      Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala
          370                375                380

      Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp
      385                390                395                400

      Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser
                  405                410                415

      Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu
              420                425                430

      Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu
          435                440                445
```

```
Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly
    450                 455             460

Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Leu Leu Ala Lys Leu Thr
465             470             475                 480

Asp Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly Arg
            485             490             495

Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys Arg
        500             505             510

Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly Ile
    515             520             525

Ile Thr Asp Lys Ile Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val Ala
    530             535             540

Glu Ala Val Leu Lys Asp Lys Lys Lys Asp Leu Ser Tyr Arg Asp Ile
545             550             555                 560

Pro Ala Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu
            565             570             575

Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe
        580             585             590

Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn
    595             600             605

Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys
    610             615             620

Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln
625             630             635                 640

Gly Arg Phe Arg Gly Gly Gly Glu Ala Pro Lys Arg Pro Ala Ala
            645             650             655

Ala Arg Glu Asp Glu Glu Arg Pro Glu Glu Glu Gly Glu Asp Glu Asp
        660             665             670

Glu Arg Glu Glu Gly Gly Gly Glu Arg Glu Pro Glu Gly Ala Arg Glu
    675             680             685

Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro
    690             695             700

Thr Ser Gly Phe His Val Asn Pro Val Val Val Phe Asp Phe Ala Ser
705             710             715                 720

Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu
            725             730             735

Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr
            740             745             750

Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His
        755             760             765

Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met
    770             775             780
```

                                      23

```
Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala
785                 790             795             800

Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser
            805             810             815

Val Tyr Gly Phe Thr Gly Ala Gln His Gly Leu Leu Pro Cys Leu His
        820             825             830

Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu Leu Ala Thr
        835             840             845

Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala
    850             855             860

Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met
865             870             875             880

Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly
            885             890             895

Leu Thr Ala Ala Gly Leu Thr Ala Val Gly Asp Lys Met Ala Ser His
        900             905             910

Ile Ser Arg Ala Leu Phe Leu Ser Pro Ile Lys Leu Glu Cys Glu Lys
        915             920             925

Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val
    930             935             940

Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys
945             950             955             960

Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu
            965             970             975

Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Ala Leu Ala Glu
        980             985             990

Arg Pro Ala Glu Glu Trp Leu Ala  Arg Pro Leu Pro Glu  Gly Leu Gln
    995             1000            1005

Ala Phe  Gly Ala Val Leu Val  Asp Ala His Arg Arg  Ile Thr Asp
    1010            1015            1020

Pro Glu  Arg Asp Ile Gln Asp  Phe Val Leu Thr Ala  Glu Leu Ser
    1025            1030            1035

Arg His  Pro Arg Ala Tyr Thr  Asn Lys Arg Leu Ala  His Leu Thr
    1040            1045            1050

Val Tyr  Tyr Lys Leu Met Ala  Arg Arg Ala Gln Val  Pro Ser Ile
    1055            1060            1065

Lys Asp  Arg Ile Pro Tyr Val  Ile Val Ala Gln Thr  Arg Glu Val
    1070            1075            1080

Glu Glu  Thr Val Ala Arg Leu  Ala Ala Leu Arg Glu  Leu Asp Ala
    1085            1090            1095

Ala Ala  Pro Gly Asp Glu Pro  Ala Pro Pro Ala Ala  Leu Pro Ser
```

24

```
        1100                    1105                    1110
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Pro Ala Lys Arg Pro Arg Glu Thr Pro Leu His Ala Asp Pro Pro
   1115   1120   1125

Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu Val Ser Glu Leu Ala
   1130   1135   1140

Glu Asp Pro Ala Tyr Ala Ile Ala His Gly Val Ala Leu Asn Thr
   1145   1150   1155

Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala Ala Cys Val Thr Phe
   1160   1165   1170

Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile Thr Glu Ser Leu Leu
   1175   1180   1185

Lys Arg Phe Ile Pro Glu Val Trp His Pro Pro Asp Asp Val Ala
   1190   1195   1200

Ala Arg Leu Arg Ala Ala Gly Phe Gly Ala Val Gly Ala Gly Ala
   1205   1210   1215

Thr Ala Glu Glu Thr Arg Arg Met Leu His Arg Ala Phe Asp Thr
   1220   1225   1230

Leu Ala
   1235

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<212> DNA
<213> herpes simplex

<400> 9
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aggcaaaact tttacaaccc ctacctcgcc ccagtcggga cgcaacagaa gccgaccggg       180

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gtcgagttta  actgtacggc  ggacaacctg  gccatcgagg  ggggcatgag  cgacctaccg     1080

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26

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cgcgaggtag aggagacggt cgcgcggctg ccgccctcc gcgagctaga cgccgccgcc    3300

ccaggggacg agcccgcccc ccccgcggcc ctgccctccc cggccaagcg ccccccgggag    3360

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gacgtggccg cgcggctccg gaccgcaggg ttcggggcgg tgggtgccgg cgctacggcg    3660

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<211> 1235
<212> PRT
<213> herpes simplex

<400> 10

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Met Phe Ser Gly Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala
1               5               10              15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala
            20              25              30

Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr
        35              40              45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg
    50              55              60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg
65              70              75              80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp
                85              90              95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg
```

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                    100                      105                      110
Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg
        115                  120                  125

Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val
        130                  135                  140

Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr
145                  150                  155                  160

Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr
                165                  170                  175

Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His
                180                  185                  190

Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn
        195                  200                  205

Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu
        210                  215                  220

Cys Glu Arg Met Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe
225                  230                  235                  240

Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr
                245                  250                  255

Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr
                260                  265                  270

Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro
        275                  280                  285

Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile
        290                  295                  300

Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro
305                  310                  315                  320

Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly
                325                       330                  335

Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile
                340                  345                  350

Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp
                355                  360                  365

Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala
        370                  375                  380

Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp
385                  390                  395                  400

Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser
                405                  410                  415

Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu
        420                  425                  430
```

```
Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu
        435                 440                 445

Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly
    450                 455                 460

Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Leu Leu Ala Lys Leu Thr
465                 470                 475                     480

Asp Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly Arg
            485                 490                 495

Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys Arg
        500                 505                 510

Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly Ile
        515                 520                 525

Ile Thr Asp Lys Ile Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val Ala
    530                 535                 540

Glu Ala Val Leu Lys Asp Lys Lys Lys Asp Leu Ser Tyr Arg Asp Ile
545                 550                 555                     560

Pro Thr Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu
            565                 570                 575

Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe
        580                 585                 590

Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn
        595                 600                 605

Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys
    610                 615                 620

Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln
625                 630                 635                     640

Gly Arg Phe Arg Gly Ala Gly Gly Glu Ala Pro Lys Arg Pro Ala Ala
            645                 650                 655

Ala Arg Glu Asp Glu Glu Arg Pro Glu Glu Glu Gly Glu Asp Glu Asn
            660                 665                 670

Glu Arg Glu Glu Gly Gly Gly Glu Arg Glu Pro Glu Gly Ala Arg Glu
        675                 680                 685

Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro
    690                 695                 700

Thr Ser Gly Phe His Val Asn Pro Val Val Val Phe Asp Phe Ala Ser
705                 710                 715                     720

Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu
            725                 730                 735

Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr
        740                 745                 750

Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His
        755                 760                 765
```

29

Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met
    770   775   780

Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala
785   790   795   800

Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser
            805   810   815

Val Tyr Gly Phe Thr Gly Ala Gln His Gly Leu Leu Pro Cys Leu His
            820   825   830

Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu Leu Ala Thr
            835   840   845

Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala
    850   855   860

Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met
865   870   875   880

Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly
            885   890   895

Leu Thr Ala Ala Gly Leu Thr Ala Val Gly Asp Lys Met Ala Ser His
            900   905   910

Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu Cys Glu Lys
    915   920   925

Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val
    930   935   940

Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys
945   950   955   960

Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu
            965   970   975

Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Ala Leu Ala Glu
            980   985   990

Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln
    995   1000   1005

Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg Ile Thr Asp
    1010   1015   1020

Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala Glu Leu Ser
    1025   1030   1035

Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala His Leu Thr
    1040   1045   1050

Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val Pro Ser Ile
    1055   1060   1065

Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr Arg Glu Val
    1070   1075   1080

Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu Leu Asp Ala

```
        1085                    1090                    1095

Ala Ala  Pro Gly Asp Glu Pro  Ala Pro Pro Ala Ala  Leu Pro Ser
        1100                   1105                  1110

Pro Ala  Lys Arg Pro Arg Glu  Thr Pro Ser Pro Ala  Asp Pro Pro
        1115                   1120                  1125

Gly Gly  Ala Ser Lys Pro Arg  Lys Leu Leu Val Ser  Glu Leu Ala
        1130                   1135                  1140

Glu Asp  Pro Ala Tyr Ala Ile  Ala His Gly Val Ala  Leu Asn Thr
        1145                   1150                  1155

Asp Tyr  Tyr Phe Ser His Leu  Leu Gly Ala Ala Cys  Val Thr Phe
        1160                   1165                  1170

Lys Ala  Leu Phe Gly Asn Asn  Ala Lys Ile Thr Glu  Ser Leu Leu
        1175                   1180                  1185

Lys Arg  Phe Ile Pro Glu Val  Trp His Pro Pro Asp  Asp Val Ala
        1190                   1195                  1200

Ala Arg  Leu Arg Thr Ala Gly  Phe Gly Ala Val Gly  Ala Gly Ala
        1205                   1210                  1215

Thr Ala  Glu Glu Thr Arg Arg  Met Leu His Arg Ala  Phe Asp Thr
        1220                   1225                  1230

Leu Ala
        1235
```

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<210>  11
<211>  3729
<212>  DNA
<213>  herpes simplex

<400>  11
atgttttca  acccgtatct  gagcggcggc  gtgaccggcg  gtgcggtcgc  gggtggccgg    60

cgtcagcgtt  cgcagcccgg  ctccgcgcag  ggctcgggca  agcggccgcc  acagaaacag   120

tttttgcaga  tcgtgccgcg  aggtgtcatg  ttcgacggtc  agacggggtt  gatcaagcat   180

aagacgggac  ggctgcctct  catgttctat  cgagagatta  aacatttgtt  gagtcatgac   240

atggtttggc  cgtgtccttg  gcgcgagacc  ctggtgggtc  gcgtggtggg  acctattcgt   300

tttcacacct  acgatcagac  ggacgccgtg  ctcttcttcg  actcgcccga  aaacgtgtcg   360

ccgcgctatc  gtcagcatct  ggtgccttcg  gggaacgtgt  tgcgtttctt  cggggccaca   420

gaacacggct  acagtatctg  cgtcaacgtt  ttcgggcagc  gcagctactt  ttactgtgag   480

tacagcgaca  ccgataggct  gcgtgaggtc  attgccagcg  tgggcgaact  agtgcccgaa   540

ccgcggacgc  catacgccgt  gtctgtcacg  ccggccacca  agacctccat  ctatgggtac   600

gggacgcgac  ccgtgcccga  tttgcagtgt  gtgtctatca  gcaactggac  catggccaga   660

aaaatcggcg  agtatctgct  ggagcagggt  tttcccgtgt  acgaggtccg  tgtggatccg   720
```

ctgacgcgtt tggtcatcga tcggcggatc accacgttcg gctggtgctc cgtgaatcgt   780

tacgactggc ggcagcaggg tcgcgcgtcg acttgtgata tcgaggtaga ctgcgatgtc   840

tctgacctgg tggctgtgcc cgacgacagc tcgtggccgc gctatcgatg cctgtccttc   900

gatatcgagt gcatgagcgg cgagggtggt tttccctgcg ccgagaagtc cgatgacatt   960

gtcattcaga tctcgtgcgt gtgctacgag acgggggggaa acaccgccgt ggatcagggg   1020

atcccaaacg ggaacgatgg tcggggctgc acttcggagg gtgtgatctt tgggcactcg   1080

ggtcttcatc tctttacgat cggcacctgc gggcaggtgg gcccagacgt ggacgtctac   1140

gagttcccctt ccgaatacga gctgctgctg ggctttatgc ttttctttca acggtacgcg   1200

ccggcctttg tgaccggtta caacatcaac tcttttgact tgaagtacat cctcacgcgt   1260

ctcgagtacc tgtataaggt ggactcgcag cgcttctgca agttgcctac ggcgcagggc   1320

ggccgtttct ttttacacag ccccgccgtg ggttttaagc ggcagtacgc cgccgctttt   1380

ccctcggctt ctcacaacaa tccggccagc acggccgcca ccaaggtgta tattgcgggt   1440

tcggtggtta tcgacatgta ccctgtatgc atggccaaga ctaactcgcc caactataag   1500

ctcaacacta tggccgagct ttacctgcgg caacgcaagg atgacctgtc ttacaaggac   1560

atcccgcgtt gtttcgtggc taatgccgag ggccgcgccc aggtaggccg ttactgtctg   1620

caggacgccg tattggtgcg cgatctgttc aacaccatta attttcacta cgaggccggg   1680

gccatcgcgc ggctggctaa aattccgttg cggcgtgtca tctttgacgg acagcagatc   1740

cgtatctaca cctcgctgct ggacgagtgc gcctgccgcg attttatcct gcccaaccac   1800

tacagcaaag gtacgacggt gcccgaaacg aatagcgttg ctgtgtcacc taacgctgct   1860

atcatctcta ccgccgctgt gcccggcgac gcgggttctg tggcggctat gtttcagatg   1920

tcgccgccct tgcaatctgc gccgtccagt caggacggcg tttcacccgg ctccggcagt   1980

aacagtagta gcagcgtcgg cgttttcagc gtcggctccg gcagtagtgg cggcgtcggc   2040

gtttccaacg acaatcacgg cgccggcggt actgcggcgg tttcgtacca gggcgccacg   2100

gtgtttgagc ccgaggtggg ttactacaac gaccccgtgg ccgtgttcga ctttgccagc   2160

ctctaccctt ccatcatcat ggcccacaac ctctgctact ccaccctgct ggtgccgggt   2220

ggcgagtacc ctgtggaccc cgccgacgta tacagcgtca cgctagagaa cggcgtgacc   2280

caccgctttg tgcgtgcttc ggtgcgcgtc tcggtgctct cggaactgct caacaagtgg   2340

gtttcgcagc ggcgtgccgt gcgcgaatgc atgcgcgagt gtcaagaccc tgtgcgccgt   2400

atgctgctcg acaaggaaca gatggcgctc aaagtaacgt gcaacgcttt ctacggtttt   2460

accggcgcgc tgaacggtat gatgccgtgt ctgcccatcg ccgccagcat cacgcgcatc   2520

ggtcgcgaca tgctagagcg cacggcgcgg ttcatcaaag acaactttttc agagccgtgt   2580

32

```
tttttgcaca atttttttaa tcaggaagac tatgtagtgg gaacgcggga gggggattcg   2640

gaggagagca gcgcgttacc ggaggggctc gaaacatcgt cagggggctc gaacgaacgg   2700

cgggtggagg cgcgggtcat ctacggggac acggacagcg tgtttgtccg ctttcgtggc   2760

ctgacgccgc aggctctggt ggcgcgtggg cccagcctgg cgcactacgt gacggcctgt   2820

ctttttgtgg agcccgtcaa gctggagttt gaaaaggtct tcgtctctct tatgatgatc   2880

tgcaagaaac gttacatcgg caaagtggag ggcgcctcgg tctgagcat gaagggcgtg   2940

gatctggtgc gcaagacggc ctgcgagttc gtcaagggcg tcacgcgtga cgtcctctcg   3000

ctgctctttg aggatcgcga ggtctcggaa gcagccgtgc gcctgtcgcg cctctcactc   3060

gatgaagtca agaagtacgg cgtgccacgc ggtttctggc gtatcttacg ccgcttggtg   3120

caggcccgcg acgatctgta cctgcaccgt gtgcgtgtcg aggacctggt gctttcgtcg   3180

gtgctctcta aggacatctc gctgtaccgt caatctaacc tgccgcacat tgccgtcatt   3240

aagcgattgg cggcccgttc tgaggagcta ccctcggtcg gggatcgggt cttttacgtt   3300

ctgacggcgc ccggtgtccg gacggcgccg cagggttcct ccgacaacgg tgattctgta   3360

accgccggcg tggtttcccg gtcggacgcg attgatggca cggacgacga cgctgacggc   3420

ggcggggtag aggagagcaa caggagagga ggagagccgg caaagaagag ggcgcggaaa   3480

ccaccgtcgg ccgtgtgcaa ctacgaggta ccgaagatc cgagctacgt gcgcgagcac   3540

ggcgtgccca ttcacgccga caagtacttt gagcaggttc tcaaggctgt aactaacgtg   3600

ctgtcgcccg tctttcccgg cggcgaaacc gcgcgcaagg acaagttttt gcacatggtg   3660

ctgccgcggc gcttgcactt ggagccggct tttctgccgt acagtgtcaa ggcgcacgaa   3720

tgctgttga                                                          3729
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<210> 12
<211> 1242
<212> PRT
<213> herpes simplex

<400> 12

```
Met Phe Phe Asn Pro Tyr Leu Ser Gly Gly Val Thr Gly Gly Ala Val
1               5                   10                  15

Ala Gly Gly Arg Arg Gln Arg Ser Gln Pro Gly Ser Ala Gln Gly Ser
                20                  25                  30

Gly Lys Arg Pro Pro Gln Lys Gln Phe Leu Gln Ile Val Pro Arg Gly
            35                  40                  45

Val Met Phe Asp Gly Gln Thr Gly Leu Ile Lys His Lys Thr Gly Arg
        50                  55                  60

Leu Pro Leu Met Phe Tyr Arg Glu Ile Lys His Leu Leu Ser His Asp
65                  70                  75                  80
```

```
Met Val Trp Pro Cys Pro Trp Arg Glu Thr Leu Val Gly Arg Val Val
              85              90                  95

Gly Pro Ile Arg Phe His Thr Tyr Asp Gln Thr Asp Ala Val Leu Phe
            100              105              110

Phe Asp Ser Pro Glu Asn Val Ser Pro Arg Tyr Arg Gln His Leu Val
        115              120              125

Pro Ser Gly Asn Val Leu Arg Phe Phe Gly Ala Thr Glu His Gly Tyr
    130              135              140

Ser Ile Cys Val Asn Val Phe Gly Gln Arg Ser Tyr Phe Tyr Cys Glu
145              150              155              160

Tyr Ser Asp Thr Asp Arg Leu Arg Glu Val Ile Ala Ser Val Gly Glu
            165              170              175

Leu Val Pro Glu Pro Arg Thr Pro Tyr Ala Val Ser Val Thr Pro Ala
        180              185              190

Thr Lys Thr Ser Ile Tyr Gly Tyr Gly Thr Arg Pro Val Pro Asp Leu
        195              200              205

Gln Cys Val Ser Ile Ser Asn Trp Thr Met Ala Arg Lys Ile Gly Glu
    210              215              220

Tyr Leu Leu Glu Gln Gly Phe Pro Val Tyr Glu Val Arg Val Asp Pro
225              230              235              240

Leu Thr Arg Leu Val Ile Asp Arg Arg Ile Thr Thr Phe Gly Trp Cys
            245              250              255

Ser Val Asn Arg Tyr Asp Trp Arg Gln Gln Gly Arg Ala Ser Thr Cys
            260              265              270

Asp Ile Glu Val Asp Cys Asp Val Ser Asp Leu Val Ala Val Pro Asp
        275              280              285

Asp Ser Ser Trp Pro Arg Tyr Arg Cys Leu Ser Phe Asp Ile Glu Cys
    290              295              300

Met Ser Gly Glu Gly Gly Phe Pro Cys Ala Glu Lys Ser Asp Asp Ile
305              310              315              320

Val Ile Gln Ile Ser Cys Val Cys Tyr Glu Thr Gly Gly Asn Thr Ala
            325              330              335

Val Asp Gln Gly Ile Pro Asn Gly Asn Asp Gly Arg Gly Cys Thr Ser
            340              345              350

Glu Gly Val Ile Phe Gly His Ser Gly Leu His Leu Phe Thr Ile Gly
        355              360              365

Thr Cys Gly Gln Val Gly Pro Asp Val Asp Val Tyr Glu Phe Pro Ser
    370              375              380

Glu Tyr Glu Leu Leu Leu Gly Phe Met Leu Phe Phe Gln Arg Tyr Ala
385              390              395              400

Pro Ala Phe Val Thr Gly Tyr Asn Ile Asn Ser Phe Asp Leu Lys Tyr
```

                    405   410   415

Ile Leu Thr Arg Leu Glu Tyr Leu Tyr Lys Val Asp Ser Gln Arg Phe
            420   425   430

Cys Lys Leu Pro Thr Ala Gln Gly Gly Arg Phe Phe Leu His Ser Pro
            435   440   445

Ala Val Gly Phe Lys Arg Gln Tyr Ala Ala Ala Phe Pro Ser Ala Ser
    450   455   460

His Asn Asn Pro Ala Ser Thr Ala Ala Thr Lys Val Tyr Ile Ala Gly
465   470   475   480

Ser Val Val Ile Asp Met Tyr Pro Val Cys Met Ala Lys Thr Asn Ser
            485   490   495

Pro Asn Tyr Lys Leu Asn Thr Met Ala Glu Leu Tyr Leu Arg Gln Arg
        500   505   510

Lys Asp Asp Leu Ser Tyr Lys Asp Ile Pro Arg Cys Phe Val Ala Asn
        515   520   525

Ala Glu Gly Arg Ala Gln Val Gly Arg Tyr Cys Leu Gln Asp Ala Val
    530   535   540

Leu Val Arg Asp Leu Phe Asn Thr Ile Asn Phe His Tyr Glu Ala Gly
545   550   555   560

Ala Ile Ala Arg Leu Ala Lys Ile Pro Leu Arg Arg Val Ile Phe Asp
            565   570   575

Gly Gln Gln Ile Arg Ile Tyr Thr Ser Leu Leu Asp Glu Cys Ala Cys
            580   585   590

Arg Asp Phe Ile Leu Pro Asn His Tyr Ser Lys Gly Thr Thr Val Pro
        595   600   605

Glu Thr Asn Ser Val Ala Val Ser Pro Asn Ala Ala Ile Ile Ser Thr
    610   615   620

Ala Ala Val Pro Gly Asp Ala Gly Ser Val Ala Ala Met Phe Gln Met
625   630   635   640

Ser Pro Pro Leu Gln Ser Ala Pro Ser Ser Gln Asp Gly Val Ser Pro
            645   650   655

Gly Ser Gly Ser Asn Ser Ser Ser Ser Val Gly Val Phe Ser Val Gly
            660   665   670

Ser Gly Ser Ser Gly Gly Val Gly Val Ser Asn Asp Asn His Gly Ala
        675   680   685

Gly Gly Thr Ala Ala Val Ser Tyr Gln Gly Ala Thr Val Phe Glu Pro
    690   695   700

Glu Val Gly Tyr Tyr Asn Asp Pro Val Ala Val Phe Asp Phe Ala Ser
705   710   715   720

Leu Tyr Pro Ser Ile Ile Met Ala His Asn Leu Cys Tyr Ser Thr Leu
            725   730   735

                                    35

Leu Val Pro Gly Gly Glu Tyr Pro Val Asp Pro Ala Asp Val Tyr Ser
            740   745   750

Val Thr Leu Glu Asn Gly Val Thr His Arg Phe Val Arg Ala Ser Val
        755   760   765

Arg Val Ser Val Leu Ser Glu Leu Leu Asn Lys Trp Val Ser Gln Arg
    770   775   780

Arg Ala Val Arg Glu Cys Met Arg Glu Cys Gln Asp Pro Val Arg Arg
785   790   795   800

Met Leu Leu Asp Lys Glu Gln Met Ala Leu Lys Val Thr Cys Asn Ala
            805   810   815

Phe Tyr Gly Phe Thr Gly Ala Leu Asn Gly Met Met Pro Cys Leu Pro
            820   825   830

Ile Ala Ala Ser Ile Thr Arg Ile Gly Arg Asp Met Leu Glu Arg Thr
            835   840   845

Ala Arg Phe Ile Lys Asp Asn Phe Ser Glu Pro Cys Phe Leu His Asn
    850   855   860

Phe Phe Asn Gln Glu Asp Tyr Val Val Gly Thr Arg Glu Gly Asp Ser
865   870   875   880

Glu Glu Ser Ser Ala Leu Pro Glu Gly Leu Glu Thr Ser Ser Gly Gly
            885   890   895

Ser Asn Glu Arg Arg Val Glu Ala Arg Val Ile Tyr Gly Asp Thr Asp
            900   905   910

Ser Val Phe Val Arg Phe Arg Gly Leu Thr Pro Gln Ala Leu Val Ala
            915   920   925

Arg Gly Pro Ser Leu Ala His Tyr Val Thr Ala Cys Leu Phe Val Glu
    930   935   940

Pro Val Lys Leu Glu Phe Glu Lys Val Phe Val Ser Leu Met Met Ile
945   950   955   960

Cys Lys Lys Arg Tyr Ile Gly Lys Val Glu Gly Ala Ser Gly Leu Ser
            965   970   :   975

Met Lys Gly Val Asp Leu Val Arg Lys Thr Ala Cys Glu Phe Val Lys
            980   985   990

Gly Val Thr Arg Asp Val Leu Ser Leu Leu Phe Glu Asp Arg Glu Val
            995   1000   1005

Ser Glu Ala Ala Val Arg Leu Ser Arg Leu Ser Leu Asp Glu Val
    1010   1015   1020

Lys Lys Tyr Gly Val Pro Arg Gly Phe Trp Arg Ile Leu Arg Arg
    1025   1030   1035

Leu Val Gln Ala Arg Asp Asp Leu Tyr Leu His Arg Val Arg Val
    1040   1045   1050

Glu Asp Leu Val Leu Ser Ser Val Leu Ser Lys Asp Ile Ser Leu
    1055   1060   1065

36

```
Tyr Arg Gln Ser Asn Leu Pro His Ile Ala Val Ile Lys Arg Leu
    1070            1075              1080

Ala Ala Arg Ser Glu Glu Leu Pro Ser Val Gly Asp Arg Val Phe
    1085            1090              1095

Tyr Val Leu Thr Ala Pro Gly Val Arg Thr Ala Pro Gln Gly Ser
    1100            1105              1110

Ser Asp Asn Gly Asp Ser Val Thr Ala Gly Val Val Ser Arg Ser
    1115            1120              1125

Asp Ala Ile Asp Gly Thr Asp Asp Asp Ala Asp Gly Gly Gly Val
    1130            1135              1140

Glu Glu Ser Asn Arg Arg Gly Gly Glu Pro Ala Lys Lys Arg Ala
    1145            1150              1155

Arg Lys Pro Pro Ser Ala Val Cys Asn Tyr Glu Val Ala Glu Asp
    1160            1165              1170

Pro Ser Tyr Val Arg Glu His Gly Val Pro Ile His Ala Asp Lys
    1175            1180              1185

Tyr Phe Glu Gln Val Leu Lys Ala Val Thr Asn Val Leu Ser Pro
    1190            1195              1200

Val Phe Pro Gly Gly Glu Thr Ala Arg Lys Asp Lys Phe Leu His
    1205            1210              1215

Met Val Leu Pro Arg Arg Leu His Leu Glu Pro Ala Phe Leu Pro
    1220            1225              1230

Tyr Ser Val Lys Ala His Glu Cys Cys
    1235            1240
```

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<210>  13
<211>  1242
<212>  PRT
<213>  herpes simplex

<400>  13
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Met Phe Phe Asn Pro Tyr Leu Ser Gly Gly Val Thr Gly Gly Ala Val
1             5               10              15

Ala Gly Gly Arg Arg Gln Arg Ser Gln Pro Gly Ser Ala Gln Gly Ser
            20              25              30

Gly Lys Arg Pro Pro Gln Lys Gln Phe Leu Gln Ile Val Pro Arg Gly
        35              40              45

Val Met Phe Asp Gly Gln Thr Gly Leu Ile Lys His Lys Thr Gly Arg
    50              55              60

Leu Pro Leu Met Phe Tyr Arg Glu Ile Lys His Leu Leu Ser His Asp
65              70              75              80

Met Val Trp Pro Cys Pro Trp Arg Glu Thr Leu Val Gly Arg Val Val
                85              90              95
```

```
Gly Pro Ile Arg Phe His Thr Tyr Asp Gln Thr Asp Ala Val Leu Phe
        100              105             110

Phe Asp Ser Pro Glu Asn Val Ser Pro Arg Tyr Arg Gln His Leu Val
        115              120             125

Pro Ser Gly Asn Val Leu Arg Phe Phe Gly Ala Thr Glu His Gly Tyr
    130              135             140

Ser Ile Cys Val Asn Val Phe Gly Gln Arg Ser Tyr Phe Tyr Cys Glu
145              150             155             160

Tyr Ser Asp Thr Asp Arg Leu Arg Glu Val Ile Ala Ser Val Gly Glu
            165             170             175

Leu Val Pro Glu Pro Arg Thr Pro Tyr Ala Val Ser Val Thr Pro Ala
        180             185             190

Thr Lys Thr Ser Ile Tyr Gly Tyr Gly Thr Arg Pro Val Pro Asp Leu
        195             200             205

Gln Cys Val Ser Ile Ser Asn Trp Thr Met Ala Arg Lys Ile Gly Glu
    210             215             220

Tyr Leu Leu Glu Gln Gly Phe Pro Val Tyr Glu Val Arg Val Asp Pro
225             230             235             240

Leu Thr Arg Leu Val Ile Asp Arg Arg Ile Thr Thr Phe Gly Trp Cys
            245             250             255

Ser Val Asn Arg Tyr Asp Trp Arg Gln Gln Gly Arg Ala Ser Thr Cys
        260             265             270

Asp Ile Glu Val Asp Cys Asp Val Ser Asp Leu Val Ala Val Pro Asp
    275             280             285

Asp Ser Ser Trp Pro Arg Tyr Arg Cys Leu Ser Phe Asp Ile Glu Cys
    290             295             300

Met Ser Gly Glu Gly Gly Phe Pro Cys Ala Glu Lys Ser Asp Asp Ile
305             310             315             320

Val Ile Gln Ile Ser Cys Val Cys Tyr Glu Thr Gly Gly Asn Thr Ala
            325             330             335

Val Asp Gln Gly Ile Pro Asn Gly Asn Asp Gly Arg Gly Cys Thr Ser
        340             345             350

Glu Gly Val Ile Phe Gly His Ser Gly Leu His Leu Phe Thr Ile Gly
        355             360             365

Thr Cys Gly Gln Val Gly Pro Asp Val Asp Val Tyr Glu Phe Pro Ser
    370             375             380

Glu Tyr Glu Leu Leu Leu Gly Phe Met Leu Phe Phe Gln Arg Tyr Ala
385             390             395             400

Pro Ala Phe Val Thr Gly Tyr Asn Ile Asn Ser Phe Asp Leu Lys Tyr
            405             410             415

Ile Leu Thr Arg Leu Glu Tyr Leu Tyr Lys Val Asp Ser Gln Arg Phe
        420             425             430
```

```
Cys Lys Leu Pro Thr Ala Gln Gly Gly Arg Phe Phe Leu His Ser Pro
        435             440             445

Ala Val Gly Phe Lys Arg Gln Tyr Ala Ala Ala Phe Pro Ser Ala Ser
        450             455             460

His Asn Asn Pro Ala Ser Thr Ala Ala Thr Lys Val Tyr Ile Ala Gly
465             470             475             480

Ser Val Val Ile Asp Met Tyr Pro Val Cys Met Ala Lys Thr Asn Ser
            485             490             495

Pro Asn Tyr Lys Leu Asn Thr Met Ala Glu Leu Tyr Leu Arg Gln Arg
            500             505             510

Lys Asp Asp Leu Ser Tyr Lys Asp Ile Pro Arg Cys Phe Val Ala Asn
            515             520             525

Ala Glu Gly Arg Ala Gln Val Gly Arg Tyr Cys Leu Gln Asp Ala Val
        530             535             540

Leu Val Arg Asp Leu Phe Asn Thr Ile Asn Phe His Tyr Glu Ala Gly
545             550             555             560

Ala Ile Ala Arg Leu Ala Lys Ile Pro Leu Arg Arg Val Ile Phe Asp
                565             570             575

Gly Gln Gln Ile Arg Ile Tyr Thr Ser Leu Leu Asp Glu Cys Ala Cys
            580             585             590

Arg Asp Phe Ile Leu Pro Asn His Tyr Ser Lys Gly Thr Thr Val Pro
            595             600             605

Glu Thr Asn Ser Val Ala Val Ser Pro Asn Ala Ala Ile Ile Ser Thr
    610             615             620

Ala Ala Val Pro Gly Asp Ala Gly Ser Val Ala Ala Met Phe Gln Met
625             630             635             640

Ser Pro Pro Leu Gln Ser Ala Pro Ser Ser Gln Asp Gly Val Ser Pro
            645             650             655

Gly Ser Gly Ser Asn Ser Ser Ser Ser Val Gly Val Phe Ser Val Gly
            660             665             670

Ser Gly Ser Ser Gly Gly Val Gly Val Ser Asn Asp Asn His Gly Ala
        675             680             685

Gly Gly Thr Ala Ala Val Ser Tyr Gln Gly Ala Thr Val Phe Glu Pro
        690             695             700

Glu Val Gly Tyr Tyr Asn Asp Pro Val Ala Val Phe Asp Phe Ala Ser
705             710             715             720

Leu Tyr Pro Ser Ile Ile Met Ala His Asn Leu Cys Tyr Ser Thr Leu
            725             730             735

Leu Val Pro Gly Gly Glu Tyr Pro Val Asp Pro Ala Asp Val Tyr Ser
            740             745             750

Val Thr Leu Glu Asn Gly Val Thr His Arg Phe Val Arg Ala Ser Val
```

```
            755                    760                    765

Arg Val Ser Val Leu Ser Glu Leu Leu Asn Lys Trp Val Ser Gln Arg
        770              775              780

Arg Ala Val Arg Glu Cys Met Arg Glu Cys Gln Asp Pro Val Arg Arg
785              790              795              800

Met Leu Leu Asp Lys Glu Gln Met Ala Leu Lys Val Thr Cys Asn Ala
                805              810              815

Phe Tyr Gly Phe Thr Gly Val Val Asn Gly Met Met Pro Cys Leu Pro
            820              825              830

Ile Ala Ala Ser Ile Thr Arg Ile Gly Arg Asp Met Leu Glu Arg Thr
        835              840              845

Ala Arg Phe Ile Lys Asp Asn Phe Ser Glu Pro Cys Phe Leu His Asn
    850              855              860

Phe Phe Asn Gln Glu Asp Tyr Val Val Gly Thr Arg Glu Gly Asp Ser
865              870              875              880

Glu Glu Ser Ser Ala Leu Pro Glu Gly Leu Glu Thr Ser Ser Gly Gly
            885              890              895

Ser Asn Glu Arg Arg Val Glu Ala Arg Val Ile Tyr Gly Asp Thr Asp
        900              905              910

Ser Val Phe Val Arg Phe Arg Gly Leu Thr Pro Gln Ala Leu Val Ala
    915              920              925

Arg Gly Pro Ser Leu Ala His Tyr Val Thr Ala Cys Leu Phe Val Glu
    930              935              940

Pro Val Lys Leu Glu Phe Glu Lys Val Phe Val Ser Leu Met Met Ile
945              950              955              960

Cys Lys Lys Arg Tyr Ile Gly Lys Val Glu Gly Ala Ser Gly Leu Ser
            965              970              975

Met Lys Gly Val Asp Leu Val Arg Lys Thr Ala Cys Glu Phe Val Lys
            980              985              990

Gly Val Thr Arg Asp Val Leu Ser Leu Leu Phe Glu Asp Arg Glu Val
        995              1000             1005

Ser Glu Ala Ala Val Arg Leu Ser Arg Leu Ser Leu Asp Glu Val
    1010             1015             1020

Lys Lys Tyr Gly Val Pro Arg Gly Phe Trp Arg Ile Leu Arg Arg
    1025             1030             1035

Leu Val Gln Ala Arg Asp Asp Leu Tyr Leu His Arg Val Arg Val
    1040             1045             1050

Glu Asp Leu Val Leu Ser Ser Val Leu Ser Lys Asp Ile Ser Leu
    1055             1060             1065

Tyr Arg Gln Ser Asn Leu Pro His Ile Ala Val Ile Lys Arg Leu
    1070             1075             1080
```

40

```
Ala Ala  Arg Ser Glu Glu Leu  Pro Ser Val Gly Asp  Arg Val Phe
    1085             1090             1095

Tyr Val  Leu Thr Ala Pro Gly  Val Arg Thr Ala Pro  Gln Gly Ser
    1100             1105             1110

Ser Asp  Asn Gly Asp Ser Val  Thr Ala Gly Val Val  Ser Arg Ser
    1115             1120             1125

Asp Ala  Ile Asp Gly Thr Asp  Asp Asp Ala Asp Gly  Gly Gly Val
    1130             1135             1140

Glu Glu  Ser Asn Arg Arg Gly  Gly Glu Pro Ala Lys  Lys Arg Ala
    1145             1150             1155

Arg Lys  Pro Pro Ser Ala Val  Cys Asn Tyr Glu Val  Ala Glu Asp
    1160             1165             1170

Pro Ser  Tyr Val Arg Glu His  Gly Val Pro Ile His  Ala Asp Lys
    1175             1180             1185

Tyr Phe  Glu Gln Val Leu Lys  Ala Val Thr Asn Val  Leu Ser Pro
    1190             1195             1200

Val Phe  Pro Gly Gly Glu Thr  Ala Arg Lys Asp Lys  Phe Leu His
    1205             1210             1215

Met Val  Leu Pro Arg Arg Leu  His Leu Glu Pro Ala  Phe Leu Pro
    1220             1225             1230

Tyr Ser  Val Lys Ala His Glu  Cys Cys
    1235             1240
```

```
<210>  14
<211>  1238
<212>  PRT
<213>  herpes simplex

<400>  14
```

```
Met Phe Cys Ala Ala Gly Gly Pro Thr Ser Pro Gly Gly Lys Ser Ala
1             5             10             15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro His Asn Pro Arg Gly Ala
            20             25             30

Thr Gln Thr Ala Pro Pro Pro Cys Arg Arg Gln Asn Phe Tyr Asn Pro
        35             40             45

His Leu Ala Gln Thr Gly Thr Gln Pro Lys Ala Pro Gly Pro Ala Gln
    50             55             60

Arg His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro
65             70             75             80

Arg Ser Leu Asp Glu Asp Ala Pro Ala Glu Gln Arg Thr Gly Val His
            85             90             95

Asp Gly Arg Leu Arg Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu
            100             105             110

Arg Asp Val Leu Arg Val Gly Pro Glu Gly Phe Trp Pro Arg Arg Leu
```

```
              115                    120                      125

    Arg Leu Trp Gly Gly Ala Asp His Ala Pro Lys Gly Phe Asp Pro Thr
        130                    135                    140

    Val Thr Val Phe His Val Tyr Asp Ile Leu Glu His Val Glu His Ala
    145                    150                    155                    160

    Tyr Ser Met Arg Ala Ala Gln Leu His Glu Arg Phe Met Asp Ala Ile
                165                    170                    175

    Thr Pro Ala Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly
                180                    185                    190

    His Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met
            195                    200                    205

    Asn Lys Ala Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp
        210                    215                    220

    Leu Cys Glu Arg Leu Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser
    225                    230                    235                    240

    Phe Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg
                245                    250                    255

    Ala Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Thr Leu Tyr Tyr Arg Val
                260                    265                    270

    Phe Val Arg Ser Gly Arg Ala Leu Ala Tyr Leu Cys Asp Asn Phe Cys
                275                    280                    285

    Pro Ala Ile Arg Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe
        290                    295                    300

    Ile Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys
    305                    310                    315                    320

    Pro Gly Arg Gly Asn Ala Pro Ala Gln Pro Arg Pro Pro Thr Ala Phe
                325                    330                    335

    Gly Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala
                340                    345                    350

    Val Glu Gly Ala Met Cys Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe
            355                    360                    365

    Asp Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val
        370                    375                    380

    Ala Glu Arg Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr
    385                    390                    395                    400

    Asp Leu Ser Thr Thr Ala Leu Glu His Ile Leu Leu Phe Ser Leu Gly
                405                    410                    415

    Ser Cys Asp Leu Pro Glu Ser His Leu Ser Asp Leu Ala Ser Arg Gly
                420                    425                    430

    Leu Pro Ala Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu
        435                    440                    445
```

```
Leu Ala Phe Met Thr Phe Val Lys Gln Tyr Gly Pro Glu Phe Val Thr
    450                 455                 460

Gly Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Val Leu Thr Lys Leu
465                 470                 475                 480

Thr Glu Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly
                485                 490                 495

Arg Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys
            500                 505                 510

Arg Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly
        515                 520                 525

Ile Ile Thr Asp Lys Val Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val
    530                 535                 540

Ala Glu Ala Val Leu Lys Asp Lys Lys Lys Asp Leu Ser Tyr Arg Asp
545                 550                 555                 560

Ile Pro Ala Tyr Tyr Ala Ser Gly Pro Ala Gln Arg Gly Val Ile Gly
            565                 570                 575

Glu Tyr Cys Val Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys
        580                 585                 590

Phe Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile
    595                 600                 605

Asn Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr
    610                 615                 620

Cys Leu Leu Arg Leu Ala Gly Gln Lys Gly Phe Ile Leu Pro Asp Thr
625                 630                 635                 640

Gln Gly Arg Phe Arg Gly Leu Asp Lys Glu Ala Pro Lys Arg Pro Ala
            645                 650                 655

Val Pro Arg Gly Glu Gly Glu Arg Pro Gly Asp Gly Asn Gly Asp Glu
            660                 665                 670

Asp Lys Asp Asp Asp Glu Asp Glu Asp Gly Asp Glu Arg Glu Glu Val
        675                 680                 685

Ala Arg Glu Thr Gly Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val
    690                 695                 700

Leu Asp Pro Thr Ser Gly Phe His Val Asp Pro Val Val Val Phe Asp
705                 710                 715                 720

Phe Ala Ser Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe
                725                 730                 735

Ser Thr Leu Ser Leu Arg Pro Glu Ala Val Ala His Leu Glu Ala Asp
            740                 745                 750

Arg Asp Tyr Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val
        755                 760                 765

Lys Ala His Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp
    770                 775                 780
```

43

Leu Ala Met Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Thr Pro
785   790   795   800

Glu Glu Ala Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val
                805   810   815

Cys Asn Ser Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu Leu Pro
            820   825   830

Cys Leu His Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu
        835   840   845

Leu Ala Thr Arg Ala Tyr Val His Ala Arg Trp Ala Glu Phe Asp Gln
    850   855   860

Leu Leu Ala Asp Phe Pro Glu Ala Ala Gly Met Arg Ala Pro Gly Pro
865   870   875   880

Tyr Ser Met Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu
            885   890   895

Cys Arg Gly Leu Thr Ala Ala Gly Leu Val Ala Met Gly Asp Lys Met
        900   905   .   910

Ala Ser His Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu
    915   920   925

Cys Glu Lys Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys Lys Tyr
    930   935   940

Ile Gly Val Ile Cys Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu
945   950   955   960

Val Arg Lys Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu
            965   970   975

Val Asp Leu Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Ala
        980   985   990

Leu Ala Glu Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu
    995   1000   1005

Gly Leu Gln Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg
    1010   1015   1020

Ile Thr Asp Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala
    1025   1030   1035

Glu Leu Ser Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala
    1040   1045   1050

His Leu Thr Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val
    1055   1060   1065

Pro Ser Ile Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr
    1070   1075   1080

Arg Glu Val Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu
    1085   1090   1095

Leu Asp Ala Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala

44

```
          1100                     1105                    1110

Leu Pro  Ser Pro Ala Lys Arg  Pro Arg Glu Thr Pro  Ser His Ala
     1115                1120                1125

Asp Pro  Pro Gly Gly Ala Ser  Lys Pro Arg Lys Leu  Leu Val Ser
     1130                1135                1140

Glu Leu  Ala Glu Asp Pro Gly  Tyr Ala Ile Ala Arg  Gly Val Pro
     1145                1150                1155

Leu Asn  Thr Asp Tyr Tyr Phe  Ser His Leu Leu Gly  Ala Ala Cys
     1160                1165                1170

Val Thr  Phe Lys Ala Leu Phe  Gly Asn Asn Ala Lys  Ile Thr Glu
     1175                1180                1185

Ser Leu  Leu Lys Arg Phe Ile  Pro Glu Thr Trp His  Pro Pro Asp
     1190                1195                1200

Asp Val  Ala Ala Arg Leu Arg  Ala Ala Gly Phe Gly  Pro Ala Gly
     1205                1210                1215

Ala Gly  Ala Thr Ala Glu Glu  Thr Arg Arg Met Leu  His Arg Ala
     1220                1225                1230

Phe Asp  Thr Leu Ala
     1235
```

<210> 15
<211> 1240
<212> PRT
<213> herpes simplex

<400> 15

```
Met Phe Cys Ala Ala Gly Gly Pro Ala Ser Pro Gly Gly Lys Ser Ala
1               5               10              15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro His Asn Pro Arg Gly Ala
            20              25              30

Thr Gln Thr Ala Pro Pro Pro Cys Arg Arg Gln Asn Phe Tyr Asn Pro
            35              40              45

His Leu Ala Gln Thr Gly Thr Gln Pro Lys Ala Pro Gly Pro Ala Gln
    50              55              60

Arg His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro
65              70              75              80

Arg Ser Leu Asp Glu Asp Ala Pro Ala Glu Gln Arg Thr Gly Val His
                85              90                  95

Asp Gly Arg Leu Arg Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu
            100             105             110

Arg Asp Val Leu Arg Val Gly Pro Glu Gly Phe Trp Pro Arg Arg Leu
        115             120             125

Arg Leu Trp Gly Gly Ala Asp His Ala Pro Glu Gly Phe Asp Pro Thr
    130             135             140
```

45

Val Thr Val Phe His Val Tyr Asp Ile Leu Glu His Val Glu His Ala
145   150   155   160

Tyr Ser Met Arg Ala Ala Gln Leu His Glu Arg Phe Met Asp Ala Ile
            165   170   175

Thr Pro Ala Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly
            180   185   190

His Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met
        195   200   205

Asn Lys Ala Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp
    210   215   220

Leu Cys Glu Arg Leu Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser
225   230   235   240

Phe Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg
            245   250   255

Ala Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Thr Leu Tyr Tyr Arg Val
            260   265   270

Phe Val Arg Ser Gly Arg Ala Leu Ala Tyr Leu Cys Asp Asn Phe Cys
        275   280   285

Pro Ala Ile Arg Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe
        290   295   300

Ile Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys
305   310   315   320

Pro Gly Arg Gly Asn Ala Pro Ala Gln Pro Arg Pro Pro Thr Ala Phe
            325   330   335

Gly Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala
            340   345   350

Val Glu Gly Ala Met Cys Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe
        355   360   365

Asp Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val
    370   375   380

Ala Glu Arg Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr
385   390   395   400

Asp Leu Ser Thr Thr Ala Leu Glu His Ile Leu Leu Phe Ser Leu Gly
            405   410   415

Ser Cys Asp Leu Pro Glu Ser His Leu Ser Asp Leu Ala Ser Arg Gly
            420   425   430

Leu Pro Ala Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu
            435   440   445

Leu Ala Phe Met Thr Phe Val Lys Gln Tyr Gly Pro Glu Phe Val Thr
    450   455   460

Gly Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Val Leu Thr Lys Leu

```
    465                 470                 475                 480

    Thr Glu Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly
                485                 490                 495

    Arg Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys
                500                 505                 510

    Arg Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly
            515                 520                 525

    Ile Ile Thr Asp Lys Val Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val
        530                 535                 540

    Ala Glu Ala Val Leu Lys Asp Lys Lys Lys Asp Leu Ser Tyr Arg Asp
    545                 550                 555                 560

    Ile Pro Ala Tyr Tyr Ala Ser Gly Pro Ala Gln Arg Gly Val Ile Gly
                565                 570                 575

    Glu Tyr Cys Val Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys
                580                 585                 590

    Phe Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile
                595                 600                 605

    Asn Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr
        610                 615                 620

    Cys Leu Leu Arg Leu Ala Gly Gln Lys Gly Phe Ile Leu Pro Asp Thr
    625                 630                 635                 640

    Gln Gly Arg Phe Arg Gly Leu Asp Lys Glu Ala Pro Lys Arg Pro Ala
                645                 650                 655

    Val Pro Arg Gly Glu Gly Glu Arg Pro Gly Asp Gly Asn Gly Asp Glu
                660                 665                 670

    Asp Lys Asp Asp Asp Glu Asp Gly Asp Glu Asp Gly Asp Glu Arg Glu
            675                 680                 685

    Glu Val Ala Arg Glu Thr Gly Gly Arg His Val Gly Tyr Gln Gly Ala
        690                 695                 700

    Arg Val Leu Asp Pro Thr Ser Gly Phe His Val Asp Pro Val Val Val
    705                 710                 715                 720

    Phe Asp Phe Ala Ser Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu
                725                 730                 735

    Cys Phe Ser Thr Leu Ser Leu Arg Pro Glu Ala Val Ala His Leu Glu
                740                 745                 750

    Ala Asp Arg Asp Tyr Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe
            755                 760                 765

    Phe Val Lys Ala His Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg
        770                 775                 780

    Asp Trp Leu Ala Met Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser
    785                 790                 795                 800
```

47

Pro Pro Glu Glu Ala Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys
            805   810   815

Val Val Cys Asn Ser Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu
            820   825   830

Leu Pro Cys Leu His Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu
        835   840   845

Met Leu Leu Ala Thr Arg Ala Tyr Val His Ala Arg Trp Ala Glu Phe
    850   855   860

Asp Gln Leu Leu Ala Asp Phe Pro Glu Ala Ala Gly Met Arg Ala Pro
865   870   875   880

Gly Pro Tyr Ser Met Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe
            885   890   895

Val Leu Cys Arg Gly Leu Thr Ala Ala Gly Leu Val Ala Met Gly Asp
        900   905   910

Lys Met Ala Ser His Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys
    915   920   925

Leu Glu Cys Glu Lys Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys
    930   935   940

Lys Tyr Ile Gly Val Ile Cys Gly Gly Lys Met Leu Ile Lys Gly Val
945   950   955   960

Asp Leu Val Arg Lys Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg
            965   970   975

Ala Leu Val Asp Leu Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala
            980   985   990

Ala Ala Leu Ala Glu Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu
        995   1000   1005

Pro Glu Gly Leu Gln Ala Phe Gly Ala Val Leu Val Asp Ala His
    1010   1015   1020

Arg Arg Ile Thr Asp Pro Glu Arg Asp Ile Gln Asp Phe Val Leu
    1025   1030   1035

Thr Ala Glu Leu Ser Arg His Pro Arg Ala Tyr Thr Asn Lys Arg
    1040   1045   1050

Leu Ala His Leu Thr Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala
    1055   1060   1065

Gln Val Pro Ser Ile Lys Asp Arg Ile Pro Tyr Val Ile Val Ala
    1070   1075   1080

Gln Thr Arg Glu Val Glu Glu Thr Val Ala Arg Leu Ala Ala Leu
    1085   1090   1095

Arg Glu Leu Asp Ala Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro
    1100   1105   1110

Ala Ala Leu Pro Ser Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser
    1115   1120   1125

48

```
His Ala  Asp Pro Pro Gly Gly  Ala Ser Lys Pro Arg  Lys Leu Leu
    1130             1135              1140

Val Ser  Glu Leu Ala Glu Asp  Pro Gly Tyr Ala Ile  Ala Arg Gly
    1145             1150              1155

Val Pro  Leu Asn Thr Asp Tyr  Tyr Phe Ser His Leu  Leu Gly Ala
    1160             1165              1170

Ala Cys  Val Thr Phe Lys Ala  Leu Phe Gly Asn Asn  Ala Lys Ile
    1175             1180              1185

Thr Glu  Ser Leu Leu Lys Arg  Phe Ile Pro Glu Thr  Trp His Pro
    1190             1195              1200

Pro Asp  Asp Val Ala Ala Arg  Leu Arg Ala Ala Gly  Phe Gly Pro
    1205 ·           1210              1215

Ala Gly  Ala Gly Ala Thr Ala  Glu Glu Thr Arg Arg  Met Leu His
    1220             1225              1230

Arg Ala  Phe Asp Thr Leu Ala
    1235             1240
```

```
<210>  16
<211>  1235
<212>  PRT
<213>  herpes simplex

<400>  16
```

```
Met Phe Ser Gly Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala
1             5             10                15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala
        20            25                30

Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr
        35            40     ·        45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg
    50            55                60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg
65            70                75                80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp
            85            90                95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg
        100           105               110

Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg
        115           120               125

Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val
    130           135               140

Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr
145           150               155               160
```

49

```
Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr
            165             170                 175

Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His
            180             185                 190

Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn
            195             200                 205

Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu
    210             215             220

Cys Glu Arg Met Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe
225             230             235                 240

Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr
            245             250             255

Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr
            260             265             270

Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro
    275             280             285

Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile
    290             295             300

Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro
305             310             315                 320

Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly
            325             330             335

Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile
            340             345             350

Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp
    355             360             365

Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala
    370             375             380

Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp
385             390             395                 400

Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser
            405             410             415

Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu
            420             425             430

Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu
            435             440             445

Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly
    450             455             460

Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Leu Leu Ala Lys Leu Thr
465             470             475                 480

Asp Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly Arg
            485             490             495
```

50

```
Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys Arg
            500             505                 510

Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly Ile
            515             520                 525

Ile Thr Asp Lys Ile Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val Ala
    530             535             540

Glu Ala Val Leu Lys Asp Lys Lys Lys Asp Leu Ser Tyr Arg Asp Ile
545             550             555                 560

Pro Ala Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu
            565             570                 575

Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe
            580             585             590

Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn
            595             600             605

Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys
    610             615             620

Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln
625             630             635                 640

Gly Arg Phe Arg Gly Ala Gly Gly Glu Ala Pro Lys Arg Pro Ala Ala
            645             650             655

Ala Arg Glu Asp Glu Glu Arg Pro Glu Glu Glu Gly Glu Asp Glu Asp
            660             665             670

Glu Arg Glu Glu Gly Gly Gly Glu Arg Glu Pro Glu Gly Ala Arg Glu
            675             680             685

Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro
    690             695             700

Thr Ser Gly Phe His Val Asn Pro Val Val Val Phe Asp Phe Ala Ser
705             710             715                 720

Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu
            725             730             735

Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr
            740             745             750

Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His
            755             760             765

Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met
    770             775             780

Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala
785             790             795                 800

Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser
            805             810             815

Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu Leu Pro Cys Leu His
```

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              820                    825                    830

Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu Leu Ala Thr
        835                    840                    845

Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala
    850                    855                    860

Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met
865                    870                    875                    880

Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly
                885                    890                    895

Leu Thr Ala Ala Gly Leu Thr Ala Met Gly Asp Lys Met Ala Ser His
                900                    905                    910

Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu Cys Glu Lys
        915                    920                    925

Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val
        930                    935                    940

Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys
945                    950                    955                    960

Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu
                965                    970                    975

Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Ala Leu Ala Glu
                980                    985                    990

Arg Pro Ala Glu Glu Trp Leu Ala  Arg Pro Leu Pro Glu  Gly Leu Gln
        995                    1000                    1005

Ala Phe  Gly Ala Val Leu Val  Asp Ala His Arg Arg  Ile Thr Asp
    1010                    1015                    1020

Pro Glu  Arg Asp Ile Gln Asp  Phe Val Leu Thr Ala  Glu Leu Ser
    1025                    1030                    1035

Arg His  Pro Arg Ala Tyr Thr  Asn Lys Arg Leu Ala  His Leu Thr
    1040                    1045                    1050

Val Tyr  Tyr Lys Leu Met Ala  Arg Arg Ala Gln Val  Pro Ser Ile
    1055                    1060                    1065

Lys Asp  Arg Ile Pro Tyr Val  Ile Val Ala Gln Thr  Arg Glu Val
    1070                    1075                    1080

Glu Glu  Thr Val Ala Arg Leu  Ala Ala Leu Arg Glu  Leu Asp Ala
    1085                    1090                    1095

Ala Ala  Pro Gly Asp Glu Pro  Ala Pro Pro Ala Ala  Leu Pro Ser
    1100                    1105                    1110

Pro Ala  Lys Arg Pro Arg Glu  Thr Pro Ser His Ala  Asp Pro Pro
    1115                    1120                    1125

Gly Gly  Ala Ser Lys Pro Arg  Lys Leu Leu Val Ser  Glu Leu Ala
    1130                    1135                    1140
```

52

```
Glu Asp  Pro Ala Tyr Ala Ile  Ala His Gly Val Ala  Leu Asn Thr
    1145             1150             1155

Asp Tyr  Tyr Phe Ser His Leu  Leu Gly Ala Ala Cys  Val Thr Phe
    1160             1165             1170

Lys Ala  Leu Phe Gly Asn Asn  Ala Lys Ile Thr Glu  Ser Leu Leu
    1175             1180             1185

Lys Arg  Phe Ile Pro Glu Val  Trp His Pro Pro Asp  Asp Val Ala
    1190             1195             1200

Ala Arg  Leu Arg Ala Ala Gly  Phe Gly Ala Val Gly  Ala Gly Ala
    1205             1210             1215

Thr Ala  Glu Glu Thr Arg Arg  Met Leu His Arg Ala  Phe Asp Thr
    1220             1225             1230

Leu Ala
    1235


<210>  17
<211>  1235
<212>  PRT
<213>  herpes simplex

<400>  17

Met Phe Ser Gly Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala
1             5             10             15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala
          20             25             30

Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr
         35             40             45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg
    50             55             60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg
65             70             75             80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp
          85             90             95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg
         100             105             110

Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg
         115             120             125

Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val
    130             135             140

Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr
145             150             155             160

Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr
              165             170             175

Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His
```

```
              180                    185                    190

Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn
        195                    200                    205

Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu
        210                    215                    220

Cys Glu Arg Met Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe
225                     230                    235                    240

Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr
                245                    250                    255

Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr
                260                    265                    270

Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro
        275                    280                    285

Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile
        290                    295                    300

Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro
305                     310                    315                    320

Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly
                325                    330                    335

Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile
                340                    345                    350

Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp
        355                    360                    365

Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala
        370                    375                    380

Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp
385                     390                    395                    400

Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser
                405                    410                    415

Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu
                420                    425                    430

Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu
        435                    440                    445

Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly
        450                    455                    460

Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Leu Leu Ala Lys Leu Thr
465                     470                    475                    480

Asp Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly Arg
                485                    490                    495

Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys Arg
                500                    505                    510
```

54

```
Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly Ile
        515             520             525

Ile Thr Asp Lys Ile Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val Ala
        530             535             540

Glu Ala Val Leu Lys Asp Lys Lys Lys Asp Leu Ser Tyr Arg Asp Ile
545             550             555             560

Pro Ala Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu
            565             570             575

Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe
            580             585             590

Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn
            595             600             605

Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys
        610             615             620

Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln
625             630             635             640

Gly Arg Phe Arg Gly Ala Gly Gly Glu Ala Pro Lys Arg Pro Ala Ala
            645             650             655

Ala Arg Glu Asp Glu Glu Arg Pro Glu Glu Glu Gly Glu Asp Glu Asp
            660             665             670

Glu Arg Glu Glu Gly Gly Gly Glu Arg Glu Pro Glu Gly Ala Arg Glu
            675             680             685

Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro
        690             695             700

Ile Ser Gly Phe His Val Asn Pro Val Val Val Phe Asp Phe Ala Ser
705             710             715             720

Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu
            725             730             735

Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr
            740             745             750

Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His
            755             760             765

Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met
        770             775             780

Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala
785             790             795             800

Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser
            805             810             815

Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu Leu Pro Cys Leu His
            820             825             830

Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu Leu Ala Thr
        835             840             845
```

55

Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala
    850   855   860

Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met
865   870   875   880

Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly
            885   890   895

Leu Thr Ala Ala Gly Leu Thr Ala Met Gly Asp Lys Met Ala Ser His
            900   905   910

Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu Cys Glu Lys
        915   920   925

Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val
    930   935   940

Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys
945   950   955   960

Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu
            965   970   975

Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Ala Leu Ala Glu
        980   985   990

Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln
    995   1000   1005

Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg Ile Thr Asp
    1010   1015   1020

Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala Glu Leu Ser
    1025   1030   1035

Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala His Leu Thr
    1040   1045   1050

Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val Pro Ser Ile
    1055   1060   1065

Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr Arg Glu Val
    1070   1075   1080

Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu Leu Asp Ala
    1085   1090   1095

Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala Leu Pro Ser
    1100   1105   1110

Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser Pro Ala Asp Pro Pro
    1115   1120   1125

Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu Val Ser Glu Leu Ala
    1130   1135   1140

Glu Asp Pro Ala Tyr Ala Ile Ala His Gly Val Ala Leu Asn Thr
    1145   1150   1155

Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala Ala Cys Val Thr Phe

56

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         1160                    1165                    1170

Lys Ala  Leu Phe Gly Asn Asn  Ala Lys Ile Thr Glu  Ser Leu Leu
    1175                1180                1185

Lys Arg  Phe Ile Pro Glu Val  Trp His Pro Pro Asp  Asp Val Thr
    1190                1195                1200

Ala Arg  Leu Arg Ala Ala Gly  Phe Gly Ala Val Gly  Ala Gly Ala
    1205                1210                1215

Thr Ala  Glu Glu Thr Arg Arg  Met Leu His Arg Ala  Phe Asp Thr
    1220                1225                1230

Leu Ala
    1235


<210>  18
<211>  1235
<212>  PRT
<213>  herpes simplex

<400>  18

Met Phe Ser Gly Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala
1               5                   10                  15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala
            20                  25                  30

Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr
        35                  40                  45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg
    50                  55                  60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg
65                  70                  75                  80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp
            85                  90                  95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg
            100                 105                 110

Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg
        115                 120                 125

Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val
    130                 135                 140

Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr
145                 150                 155                 160

Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr
            165                 170                 175

Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His
            180                 185                 190

Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn
        195                 200                 205
```

```
Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu
    210             215             220

Cys Glu Arg Met Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe
225             230             235             240

Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr
            245             250             255

Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr
            260             265             270

Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro
        275             280             285

Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile
    290             295             300

Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro
305             310             315             320

Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly
            325             330             335

Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile
            340             345             350

Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp
        355             360             365

Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala
    370             375             380

Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp
385             390             395             400

Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser
            405             410             415

Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu
            420             425             430

Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu
        435             440             445

Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly
    450             455             460

Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Leu Leu Ala Lys Leu Thr
465             470             475             480

Asp Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly Arg
            485             490             495

Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys Arg
            500             505             510

Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly Ile
        515             520             525

Ile Thr Asp Lys Ile Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val Ala
```

```
        530                    535                      540

Glu Ala Val Leu Lys Asp Lys Lys Asp Leu Ser Tyr Arg Asp Ile
545                 550              555                  560

Pro Thr Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu
                565              570              575

Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe
            580              585              590

Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn
            595              600              605

Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys
    610              615              620

Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln
625              630              635                  640

Gly Arg Phe Arg Gly Ala Gly Gly Glu Ala Pro Lys Arg Pro Ala Ala
            645              650              655

Ala Arg Glu Asp Glu Glu Arg Pro Glu Glu Glu Gly Glu Asp Glu Asn
            660              665              670

Glu Arg Glu Glu Gly Gly Gly Glu Arg Glu Pro Glu Gly Ala Arg Glu
        675              680              685

Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro
    690              695              700

Thr Ser Gly Phe His Val Asn Pro Val Val Val Phe Asp Phe Ala Ser
705              710              715                  720

Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu
            725              730              735

Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr
            740              745              750

Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His
            755              760              765

Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met
    770              775              780

Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala
785              790              795                  800

Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser
            805              810              815

Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu Leu Pro Cys Leu His
            820              825              830

Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu Leu Ala Thr
            835              840              845

Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala
    850              855              860
```

```
Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met
865             870             875             880

Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly
            885             890             895

Leu Thr Ala Ala Gly Leu Thr Ala Val Gly Asp Lys Met Ala Ser His
            900             905             910

Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu Cys Glu Lys
        915             920             925

Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val
    930             935             940

Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys
945             950             955             960

Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu
            965             970             975

Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Ala Leu Ala Glu
            980             985             990

Arg Pro Ala Glu Glu Trp Leu Ala  Arg Pro Leu Pro Glu  Gly Leu Gln
        995             1000            1005

Ala Phe  Gly Ala Val Leu Val  Asp Ala His Arg Arg  Ile Thr Asp
    1010            1015            1020

Pro Glu  Arg Asp Ile Gln Asp  Phe Val Leu Thr Ala  Glu Leu Ser
    1025            1030            1035

Arg His  Pro Arg Ala Tyr Thr  Asn Lys Arg Leu Ala  His Leu Thr
    1040            1045            1050

Val Tyr  Tyr Lys Leu Met Ala  Arg Arg Ala Gln Val  Pro Ser Ile
    1055            1060            1065

Lys Asp  Arg Ile Pro Tyr Val  Ile Val Ala Gln Thr  Arg Glu Val
    1070            1075            1080

Glu Glu  Thr Val Ala Arg Leu  Ala Ala Leu Arg Glu  Leu Asp Ala
    1085            1090            1095

Ala Ala  Pro Gly Asp Glu Pro  Ala Pro Pro Ala Ala  Leu Pro Ser
    1100            1105            1110

Pro Ala  Lys Arg Pro Arg Glu  Thr Pro Ser Pro Ala  Asp Pro Pro
    1115            1120            1125

Gly Gly  Ala Ser Lys Pro Arg  Lys Leu Leu Val Ser  Glu Leu Ala
    1130            1135            1140

Glu Asp  Pro Ala Tyr Ala Ile  Ala His Gly Val Ala  Leu Asn Thr
    1145            1150            1155

Asp Tyr  Tyr Phe Ser His Leu  Leu Gly Ala Ala Cys  Val Thr Phe
    1160            1165            1170

Lys Ala  Leu Phe Gly Asn Asn  Ala Lys Ile Thr Glu  Ser Leu Leu
    1175            1180            1185
```

```
Lys Arg  Phe Ile Pro Glu Val  Trp His Pro Pro Asp  Asp Val Ala
    1190                 1195                 1200

Ala Arg  Leu Arg Thr Ala Gly  Phe Gly Ala Val Gly  Ala Gly Ala
    1205                 1210                 1215

Thr Ala  Glu Glu Thr Arg Arg  Met Leu His Arg Ala  Phe Asp Thr
    1220                 1225                 1230

Leu Ala
    1235
```

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<210>  19
<211>  1235
<212>  PRT
<213>  herpes simplex

<400>  19
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```
Met Phe Ser Gly Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala
1               5               10              15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala
            20              25              30

Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr
        35              40              45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg
    50              55              60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg
65              70              75              80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp
            85              90              95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg
        100             105             110

Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg
        115             120             125

Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val
    130             135             140

Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr
145             150             155             160

Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr
            165             170             175

Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His
        180             185             190

Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn
    195             200             205

Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu
    210             215             220
```

```
Cys Glu Arg Met Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe
225             230             235             240

Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr
            245             250             255

Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr
        260             265             270

Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro
        275             280             285

Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile
    290             295             300

Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro
305             310             315             320

Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly
            325             330             335

Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile
        340             345             350

Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp
        355             360             365

Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala
    370             375             380

Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp
385             390             395             400

Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser
            405             410             415

Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu
        420             425             430

Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu
        435             440             445

Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly
    450             455             460

Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Leu Leu Ala Lys Leu Thr
465             470             475             480

Asp Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly Arg
            485             490             495

Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys Arg
        500             505             510

Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly Ile
        515             520             525

Ile Thr Asp Lys Ile Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val Ala
    530             535             540

Glu Ala Val Leu Lys Asp Lys Lys Lys Asp Leu Ser Tyr Arg Asp Ile
545             550             555             560
```

62

```
Pro Ala Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu
            565             570             575

Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe
            580             585             590

Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn
            595             600             605

Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys
    610             615             620

Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln
625             630             635             640

Gly Arg Phe Arg Gly Gly Gly Gly Glu Ala Pro Lys Arg Pro Ala Ala
            645             650             655

Ala Arg Glu Asp Glu Glu Arg Pro Glu Glu Glu Gly Glu Asp Glu Asp
            660             665             670

Glu Arg Glu Glu Gly Gly Gly Glu Arg Glu Pro Glu Gly Ala Arg Glu
            675             680             685

Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro
    690             695             700

Thr Ser Gly Phe His Val Asn Pro Val Val Val Phe Asp Phe Ala Ser
705             710             715             720

Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu
            725             730             735

Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr
            740             745             750

Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His
            755             760             765

Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met
    770             775             780

Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala
785             790             795             800

Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser
            805             810             815

Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu Leu Pro Cys Leu His
            820             825             830

Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu Leu Ala Thr
            835             840             845

Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala
    850             855             860

Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met
865             870             875             880

Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly
```

```
              885                  890                  895

Leu Thr Ala Ala Gly Leu Thr Ala Val Gly Asp Lys Met Ala Ser His
            900              905              910

Ile Ser Arg Ala Leu Phe Leu Ser Pro Ile Lys Leu Glu Cys Glu Lys
        915              920              925

Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val
    930              935              940

Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys
945              950              955              960

Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu
                965              970              975

Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Ala Leu Ala Glu
            980              985              990

Arg Pro Ala Glu Glu Trp Leu Ala  Arg Pro Leu Pro Glu  Gly Leu Gln
        995              1000              1005

Ala Phe  Gly Ala Val Leu Val  Asp Ala His Arg Arg  Ile Thr Asp
    1010              1015              1020

Pro Glu  Arg Asp Ile Gln Asp  Phe Val Leu Thr Ala  Glu Leu Ser
    1025              1030              1035

Arg His  Pro Arg Ala Tyr Thr  Asn Lys Arg Leu Ala  His Leu Thr
    1040              1045              1050

Val Tyr  Tyr Lys Leu Met Ala  Arg Arg Ala Gln Val  Pro Ser Ile
    1055              1060              1065

Lys Asp  Arg Ile Pro Tyr Val  Ile Val Ala Gln Thr  Arg Glu Val
    1070              1075              1080

Glu Glu  Thr Val Ala Arg Leu  Ala Ala Leu Arg Glu  Leu Asp Ala
    1085              1090              1095

Ala Ala  Pro Gly Asp Glu Pro  Ala Pro Pro Ala Ala  Leu Pro Ser
    1100              1105              1110

Pro Ala  Lys Arg Pro Arg Glu  Thr Pro Leu His Ala  Asp Pro Pro
    1115              1120              1125

Gly Gly  Ala Ser Lys Pro Arg  Lys Leu Leu Val Ser  Glu Leu Ala
    1130              1135              1140

Glu Asp  Pro Ala Tyr Ala Ile  Ala His Gly Val Ala  Leu Asn Thr
    1145              1150              1155

Asp Tyr  Tyr Phe Ser His Leu  Leu Gly Ala Ala Cys  Val Thr Phe
    1160              1165              1170

Lys Ala  Leu Phe Gly Asn Asn  Ala Lys Ile Thr Glu  Ser Leu Leu
    1175              1180              1185

Lys Arg  Phe Ile Pro Glu Val  Trp His Pro Pro Asp  Asp Val Ala
    1190              1195              1200
```

```
Ala Arg Leu Arg Ala Ala Gly  Phe Gly Ala Val Gly  Ala Gly Ala
    1205        1210              1215
```

```
Thr Ala Glu Glu Thr Arg Arg  Met Leu His Arg Ala  Phe Asp Thr
    1220        1225              1230
```

```
Leu Ala
    1235
```